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PHILIPPINE FIBERS AND FIBROUS SUBSTANCES: THEIR SUITABILITY FOR PAPER MAKING.

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(From the Chemical Laboratory, Bureau of Science.)

RAW MATERIALS FOR PAPER MAKING.

Introduction.—From the earliest Egyptian papyrus to the paper of to-day, the predominant characteristic of this material is that it consists of the enduring portions of vegetable growth known as cellulose, although animal and mineral fibers such as wool, silk, and asbestos are occasionally employed. The art of modern paper making consists of uniting or felting together any fibrous material so as to form a continuous sheet. Linen or cotton rags are no longer exclusively employed; indeed, these substances at present constitute but a small fraction of the raw material of the paper-making industry. Any vegetable matter possessing sufficient fibrous structure can be utilized.[1]

Notwithstanding the great variety of available cheap materials, rags of various kinds continued to form the chief substances for paper making both in Europe and America, until the middle of the nineteenth century, at which time they ceased to be obtainable in sufficient quantities to supply the demand and paper makers began to search elsewhere for a cheaper and more inexhaustible material for their rapidly growing industry. In 1854 wood-pulp was first used in the United States, and

[1] "In order to give some idea of the variety of materials from which paper can be and has been prepared, we may cite a book published in 1765 at Regensburg, Germany, by Jacob Schaeffer, the paper of which was made from about sixty different sources, among which the following are curious and interesting examples: Sawdust, hop vines, hornets' nests, peat, straw, cabbage stumps, moss, and thistle stalks." Thorpe: *Dictionary Applied Chemistry*, 3, 105.

three years later Mr. Thomas Routledge introduced esparto grass into England. The simultaneous introduction of wood and grass furnished the first important sources of raw material for paper making and provided the first evidence that perennial grasses are suitable for paper stock.[2]

It is interesting to note the direction which search for suitable paper material was taking when the adaptability of wood for this purpose was first discovered and also to predict the lines of future inquiry when wood no longer meets the demand. When, in 1861, all import duties in Great Britain were repealed, the resulting establishment of a vast number of weekly and daily papers and journals created so great a demand for paper and paper pulp that manufacturers were forced to supplement the imported Spanish and North African esparto grass with the cereal straws, but even these proved insufficient to meet the requirements and, as the prosperity of English paper mills appeared to be at stake, the demand seemed justified that the Indian bamboo forests be thrown open to private enterprise; accordingly, Mr. Thomas Routledge, a prominent paper manufacturer of Sunderland to whom the introduction of esparto is due, sent investigators to India to study the problem in that country. However, about this time the manufacture of paper stock from spruce timber had been developed on the Continent, particularly in Germany and Sweden, and supplies of this new material from those countries brought the much-needed relief; nevertheless, experiments were carried far enough to demonstrate that bamboo fiber is much superior to spruce for paper stock and there seems but little doubt that the bamboo-paper question eventually will be reopened.

In America the evolution of raw material for paper making followed somewhat different lines. The transition from rags to wood was direct and was later followed by the use of straw in those regions far removed from the spruce forests. No recourse to perennial grasses or bamboo has thus far been necessary.

For half a century wood-pulp has met the rapidly increasing demand for paper stock. However, we are now confronted with the fact that the supply of this material will soon be exhausted, so that we are afforded a curious example of the manner in which the development of an industry sometimes brings one back to the conditions of the beginning, although the new point reached, owing to the persistence of scientific inquiry which was undertaken regardless of an utter lack of apparent practical benefit, is on a much higher plane.

Until wood-pulp had been proven to be suitable for paper stock, the world's supply of fibrous material was divided between the textile and paper industries, one being complementary to the other. Such vegetable

[2] As fibers of cotton and flax in the form of cotton and linen rags have already undergone purification and have been subjected to processes of manufacture, they can not, strictly speaking, be considered as raw materials.

fibers as cotton, hemp, jute, flax, and abacá are eminently suited for the manufacture of paper, but their primary value for textiles and cordage excluded their use in the raw state for paper and therefore, the paper makers obtained their material largely from the refuse of these industries. Good cotton and linen rags have become a luxury in the paper-making world. They are only indulged in now for making the best class of stationery, and by fortunate coincidence, this is about the only use to which they can be put. At first glance, wood might be considered too valuable for other purposes, but fortunately, those varieties which find most favor for the making of paper pulp are considered rather worthless for the many other uses for which wood is usually employed; furthermore, the demands of the spinner and cordage maker need not be considered. Twenty or twenty-five years ago statements "that there is not the slightest ground for believing the supply of this raw material would ever fail" were common in regard to wood as a material for paper making. The marvelous growth in the paper industry of the last two decades was not then foreseen nor were the many other uses for wood-pulp, which modern advances in the industrial world have brought about, taken into account.

P. H. Clutterbuck, referring to the numberless uses of wood-pulp, writes:[3]

> Printing paper alone eats an enormous hole in our natural forests yearly and the future requirements can only be conjectured. The huge procession of railway cars all over the country run, to some extent, on paper wheels; carpenters are beginning to use boards of paper, handsomely veined, requiring no planing, twice as durable as the wooden variety and costing only half the money. The builder is introducing paper bricks, showily enameled, which will not burn and possess many advantages over those of clay. The shipbuilder introduces masts and spars of the same substance, which is likewise used for telegraph and telephone poles and flagstaffs. These are not fanciful experiments but serious business procedures, justified by superior durability of the articles so produced. This same quality is claimed for the paper horseshoe recently invented and so extensively used.

Already, paper manufacturers in the United States are looking for new sources of supply for raw material. A recent report of the United States Department of Agriculture[4] recommends that investigations be made on the suitability of new raw materials for paper and paper pulp.

"Our well-known pulp woods are being used up faster than they are growing, and as a consequence the demand for new material has led to efforts to utilize many waste products among which bagasse or sugar-cane refuse, cornstalks, southern pine waste, rice straw, and hemp stalks present exceeding promising fields."

The United States Government recently has established a laboratory at Washington for investigations along these lines, and this fact emphasizes the importance which the question is assuming.

[3] P. H. Cutterbuck: *Indian Forester* (1899), **25**, 231.

[4] U. S. Department Agrl.: *The report of the Chemist* (1904).

PULP AND PAPER MAKING.

During the nineteenth century there were remarkable changes and improvements in the methods employed for converting paper stock into paper pulp and paper. These advances have been due to two causes—one, the revolution in the nature and supply of the raw material itself, and the other, the increased demand for the finished product. The method of preparation of paper pulp or half-stuff has thus far largely been dependent upon the nature of the material treated, whereas the making of the pulp into finished paper in sufficient quantities to meet the marvelous growth of the industry has caused the laborious hand process to be superseded by the huge automatic machines of the present time. However, the principles involved in the making of paper remain unaltered, regardless of whether the material is removed from a vat with a small hand sieve and turned out a single sheet at a time or is allowed to flow on to an endless wire cloth web under heavy rolls and over the steam-heated drying cylinders of a Fourdrinier machine. Generally speaking, the purpose is just the opposite of that which obtains in the isolation of fibers for the textile and cordage industries; instead of so treating the fibrous substance as to preserve the fiber bundles or filaments in their greatest length, it is necessary, by some mechanical or chemical means, to convert them into the individual fibers or cells of which the filaments are composed.

There are five distinct steps in the preparation of paper pulp from any vegetable material. Two of these are entirely mechanical, whereas the remainder are of a distinctly chemical nature. Arranged in their order of procedure, they are:

1. *Cleaning.*—A purely mechanical process which consists in removing all foreign matter such as sand, dirt, weeds, chaff, etc., either by hand or machinery.

2. *Boiling or digesting.*—This results in eliminating the soluble plant constituents and incrusting matter by chemical means.

3. *Bleaching* consists in further chemically purifying the resistant cellulose by removing adhering coloring matter.

4. *Beating or refining.*—This procedure mechanically disintegrates the pulpy mass of fibers into fragments of requisite length.

5. *Loading, sizing, and coloring* so modify the bleached and beaten pulp by the addition of mineral or animal substances, that a nonporous, resistant surface of the required shade is given to the finished product.

BOILING OR DIGESTING.

At the present time there are two main groups of processes in general use for the isolation of paper cellulose, namely, the alkaline and acid treatments. The first and older method depends upon the action of solutions of caustic soda, soda ash, caustic lime, or mixtures of these

chemicals, under varying conditions of strength of solution, pressure, and duration of digestion.[5] Therefore it is evident that in valuing an unknown material for use as paper stock these differences need carefully to be considered.

The second method for the resolution of raw fibers is of comparatively recent origin and consists in cooking them under strong pressure with sulphurous acid, either free or combined with soda, lime, or magnesia in the form of the bisulphites of these bases. The development of this process has been slow, owing to the many mechanical difficulties involved, the strong chemicals employed attacking and soon rendering the digesters worthless. However, within recent years resistant digester linings have been invented and now this process is established as the leading method for the preparation of chemical wood-pulp. Comparatively little has been done to show its adaptability to materials other than wood, but the process has so many features of superiority over the alkaline one that its application in the treatment of various other materials will be considered in a subsequent paper when work on the value of Philippine woods for paper stock will be reviewed.[6]

Bleaching of paper pulp.—All fibers do not act alike with bleaching agents. Jute, for example, does not bleach white by any known method which does not also seriously injure the fiber, while other substances require varying proportions of bleach liquor and special conditions of treatment to secure satisfactory results. Therefore, it is important to subject new, raw materials to quantitative bleach operations in order to determine the right method of procedure and the amount of bleaching powder required. The loading, sizing and coloring of paper are not materially affected by the source from which the pulp is derived and need only concern us here with respect to the kinds of chemicals in general use for these purposes and the possibilities of obtaining them in the local market. The question of chemicals for this and the other steps in the process of pulp manufacture is an important one and will thoroughly be discussed in a later number of this journal.

VEGETABLE FIBERS.

Botanical classification of fiber-producing plants.—Fiber plants are included in two great divisions of the vegetable kingdom—i. e., Dicotyle-

[5] Esparto grass is invariably subjected to the alkaline method of treatment, but the pressures carried vary from 5 to 50 pounds, the time of digestion from one to six and one-half hours and the strength of the caustic liquor from 10 to 20 per cent, calculated upon the gross weight of the material.

[6] "On account of the considerable proportion of silica present in straw, it has generally been assumed that this material would not easily lend itself to treatment by the sulphite process. Practical experience has, however, shown that this is not the case, and this process has recently been applied to the preparation of straw pulp with excellent results." Griffin & Little: *Chem. of Paper Making*, 161.

dons and Monocotyledons. The most evident characteristic of these two great divisions of plants is found in the arrangement of the leaf veins. Dicotyledonous plants are characterized by netted-veined leaves, whereas the monocotyledonous ones may usually be identified by leaves with parallel veins. The chief fiber-yielding families of the first division are:

Linaceæ; Flax family; example, flax.

Malvaceæ; example, cotton.

Tiliaceæ; example, jute.

Urticaceæ or nettle family; example, hemp.

Moraceæ; example, mulberry.

Of the second division the *Gramineæ* or Grass family, *Liliaceæ, Palmæ,* or Palm family, and *Musaceæ* or Plantain family are the more important orders of fiber producers. While a number of netted-veined, fibrous plants such as ramie and jute are distinctly tropical in habitat, only a few unimportant species are found in the Philippines, and hence it appears that families of Monocotyledons are the only ones represented by plants of commercial importance in these Islands.

Structural classification.—With the exception of fibers like cotton, kapok, etc., which are unicellular seed hairs and termed *surface fibers,* practically all fibers may structurally be classified according to the two main groups of families from which they are derived. The dicotyledonous plants produce the so-called *bast fibers,* contained in the inner fibrous bark of stems and twigs, while on the other hand the commercial fibers of monocotyledonous plants are generally found distributed throughout the entire stem, where they form the framework which gives rigidity and toughness to the plant structure, and hence they are termed *structural fibers.* Such fibers occur in the sheathing leafstalks of plantains, in the fleshy leaves of maguey and pineapple, and in the leaves and stalks of palms and grasses.

Economic classification.—A descriptive catalogue of the useful fiber plants of the world by C. R. Dodge[7] enumerates over one thousand species, the more important of which are fully described and treated from the botanical, structural, and industrial standpoints. His classification of fiber plants based on their uses is both so simple and natural that we incorporate its main features, at the same time drawing on local fiber plants for illustrating the numerous divisions of the scheme:

A. *Spinning fibers.*
   1. Fabric fibers; pineapple, abacá, ramie, etc.
   2. Netting fibers; palms, rattan, bamboo.
   3. Cordage fibers; abacá, maguey, bamboo, rattan.

B. *Tie material* (rough twisted). Palms, rattans, bamboos, grasses.

C. *Natural textiles.* Fibrous sheaths of palms.

D. *Brush fibers.* Palm fibers, bamboo.

[7] *Report No.* 9, U. S. Department of Agriculture.

E. *Plaiting and rough weaving fibers.*

1. Articles for attire; hats, sandals, etc. Abacá, palms, bamboo.
2. Mats and mattings; also thatch materials. Grasses, bamboos, palms, etc.

F. *Forms of filling.* Kapok, straw, grasses.

G. *Paper material.*

1. Textile papers. All waste from A, including old rope.
2. Bast papers.
3. Palm papers. From the fibrous material of palms and similar monocotyledonous plants, including rattans.
4. Bamboo and grass papers. This includes all material from graminaceous plants, including bamboos, cereal straws, and true grasses.
5. Wood pulp papers. Philippine soft woods, Lauan (*Shorea*), Cupang (*Parkia*), *Grewia*, etc.

It will be seen from this scheme of classification and from the native plants selected to exemplify each division of use, first, that a comparatively small number of plants supply fiber for all the present requirements; for instance, plantains, grasses, bamboo, rattan, and palm fiber are made into fabrics, fish nets, hats, baskets, mats, twine, rope, thatch, brushes, and brooms; second, that those plants which find such general use are without exception monocotyledons and their fibers are of the class termed *structural;* third, that with the exception of maguey and pineapple they are either plantains, grasses, or palms; fourth, that, leaving out of consideration native woods as a possible source of paper stock, the available supply of material for any future paper industry in the Philippines must come from one or more of these three sources.[8]

Chemical examination of raw material.—In making a study of an unknown, fibrous substance with the view of determining its possible utilization for paper stock, the three most important points to be considered are, first, its cellulose content, namely, the percentage of pulp which a given raw material will yield; second, the ease with which it responds to the ordinary cooking and bleaching processes necessary for its conversion into paper pulp; and third, the physical characteristics of the individual fibers—that is, the nature of the fiber bundles and the dimensions of the ultimate fibers of which they are composed. If the above information is favorable—namely, if the raw material is relatively high in resistant cellulose; if it is easily reduced and readily bleached, taking into account the strength of liquors required; if the ultimate fibers are found to be long and thin, with tapering, curly ends—then the question of distribution, availability, and cost of collection of that raw material is well worth careful consideration. While a quantitative determination of cellulose on a 5-gram sample of material affords some basis for estimating the amount of paper pulp it will produce, the results thus

[8] Maguey culture is rapidly increasing in northern Luzon, and the waste from the stripping of the plant may become an important factor in paper making.

obtained [9] are invariably much higher than those recorded in the factory, where much loss of fiber due to the practical, time-saving methods in vogue, is inevitable. Furthermore, many raw materials—abacá waste, for instance—are of such a nature as to render the taking of a small, representative sample practically impossible.

The method adopted in the laboratory for determining the percentage of cellulose or paper pulp is that used on a larger scale in the factory—i. e., severe alkaline digestion at elevated temperatures. It is also true that the ease with which the cellulose may be obtained can only properly be established by direct experimentation under factory conditions. To meet these, we had constructed a model digester of sufficient capacity to accommodate several pounds of material and so arranged that it could be converted for use with alkali or sulphite liquors, with the necessary steam and temperature gauges for carrying out digestions at elevated pressures.

Proceeding with the chemical examination of a given fibrous substance, there are other questions to be determined before the value of a raw material as a source of paper stock is fully expressed. Besides knowing the proportion of paper cellulose contained in the material to be considered and the ease with which it may be isolated, it is necessary to form some idea of its chemical nature—i. e., its general composition and behavior with hydrolytic and oxidizing agents—for on such knowledge our ideas of the purity and stability of the manufactured product are based.

PHILIPPINE FIBERS.

In looking over the field for suitable material for purposes of study, our attention was first directed to abacá, or Manila hemp, as it sometimes is termed. This plant is a species of wild banana of which there are several indigenous to, or introduced into, the Philippine Islands, and, as is well known, so-called Manila paper has long been made from worn-out ropes of this fiber. Its superior quality for the manufacture of special kinds of paper where strength is the desideratum is well demonstrated.

According to the Twelfth Report of the United States Census, American paper manufacturers purchased approximately 100,000 tons of so-called Manila stock for use in their mills; the approximate cost was $2,500,000, or $25 per ton. This stock was made up of old, worn-out rope, gunny sacks, waste thread, and binder twine, and it includes jute

	[9] *Laboratory method.* (Yield of dry cellulose on dry raw material.)	*Paper maker's method.* (Yield of air-dry pulp on air-dry raw material.)
	Per cent.	Per cent.
Esparto	50–55	43–47
Straw	50–55	33–37
Wood	50–50	35–43

Cross and Bevan: *Cellulose*, 284.

butts and waste. Rags, which the world over are considered to be the finest material for paper making, do not command a much greater price. In the same census year (1900) 234,000 tons of rags valued at $6,600,000, equal to about $28 per ton, were used. Statistics also show an annual output of 90,000 tons of Manila wrapping paper valued at $66 per ton and 204,000 tons of "bogus" Manila paper made from wood, rated at $9,150,000, or $45 per ton. A large proportion of the so-called Manila wrappers, paper, and envelopes contain mechanical or ground wood, which causes such articles to deteriorate and to turn brown with age. G. E. Marshall, of Turners Falls, Massachusetts, has patented a process for giving the characteristic color of Manila stock to wood-pulp and such attempts at imitation and adulteration show very conclusively the repute in which real abacá stock is held.

Abacá waste.—It has been observed for a long time that much fiber is lost in the ordinary hand processes for isolating the cordage fiber from this plant, and, in 1887, some of this waste from abacá was sent to Messrs. Gonzales Sons, of Barcelona, Spain, who reported as follows:

> Observations made in the course of fabrication permit us to affirm roundly that abacá waste as raw material for the manufacture of paper is not only utilizable but surpasses esparto and hemp, and, in its treatment for conversion into paper, excels rags and other material known in the industry.

In 1888, Sr. D. José Jordana published a small pamphlet entitled "El Abacá," containing a specimen sheet of paper made from abacá waste and also a section devoted to the application of this material for the manufacture of paper, from which the following brief extract is taken:

> As with all vegetable filaments, excellent paper can be made with abacá, even though this use is not made of it on account of its greater value as a textile. The waste which remains after removing the pulpy envelope could also be used for this manufacture. This envelope is left in the fields in its entirety, where it serves only as fertilizer for the plants; and on account of the imperfections of the method of extraction the quantity of this is so great that it exceeds 75 per cent of the total of the solid part harvested. In any case, industry and commerce should give attention to this matter. The abundance, cheapness, and excellence of a raw material are guaranties of all industrial enterprises, and this condition is found to-day in abacá waste.

In 1904, a quantity of this waste material was sent to the Everett Pulp and Paper Company, of Everett, Washington, U. S. A., for further opinion as to its adaptability for paper manufacture. Through the courtesy of the Bureau of Agriculture of the Philippine Islands we give the chemist's report:

> The waste as received was very dirty, and could not be used in the way we now treat our wood, but would have to be passed through a duster or "Devil," such as is used for very dirty rags, oakum, rope, etc. It may be possible in collecting this material to avoid a large part of this dirt.

The waste was submitted to the same process as the wood now being used, except the caustic-soda solution was one-half the strength, the time of digesting four and one-half hours, the pressure 100 pounds, and 325° Fahrenheit temperature.

The cooking was done by indirect steam—that is, the heat was produced by a steam coil in the digester, and not direct steam as we use it.

The fiber reduces very easily, and, after being washed in hot water, bleaches to color of sample, with the same amount of bleaching powder as required by the wood pulp.

The loss in the process from the dry, crude material to the dry, bleached pulp is 64 per cent, or, the crude material will produce 36 per cent by weight of fiber ready for the beater.

Under the microscope the fibers are long, slender, and smooth, tapering to a point at the ends; some have small hairs on the sides.

The bleached fiber contained 6.8 per cent ash, while wood fiber has less than 2 per cent and in most instances when well cooked has only 0.3 per cent.

This however, does not detract from the value as a paper-making material.

Owing to the small amount of material received, it has been impossible for me to try any experiments along the line of obtaining the same results by the use of cheaper chemicals. It might be possible to do the work with a solution of lime, the same as straw is treated.

In my opinion this abacá waste can be reduced to a fine, silky fiber, suitable for the best of paper, making a sheet equal to the best linen, or without being bleached, made into a light-gray wrapping paper, which would excel in strength any paper on the market.

In the meantime, the Bureau of Agriculture of the Philippine Islands conducted a series of experiments in stripping abacá by the customary hand process for the purpose of determining the relative amounts of dry cordage fiber saved and dry fibrous waste lost.[10]

Weight.	San Ramon, Mindanao.	Paete, Laguna.
Weight of green stalk ---------- kilos	9.525	15.876
Weight of green fiber ---------- do	.4536	.680
Weight of dry fiber ---------- do	.163	.2268
Weight of green fibrous waste ---------- do	1.814	2.494
Weight of dry fibrous waste ---------- do	.1769	.199
Percentage of dry waste in stalk ----------	1.85	1.25
Percentage of dry fiber in stalk ----------	1.7	1.43

The importance of the above data because they seriously influence our judgment of the supply of this waste material, justifies their repetition, particularly as we also subsequently desired to learn the effect of machine stripping on stalks under the same conditions. The following table gives a comparison between the hand and machine stripping processes; the stalks used were from Paete, Laguna, and had been harvested about two

[10] *Report* of H. T. Edwards, Fiber Expert, Bureau of Agriculture, Manila, P. I. (1904).

weeks before the tests were made. The results are averaged from ten stalks:

Weight.	Hand stripped.	Machine stripped.
Green stalk.....kilos..	15.876	13.984
Green fiber.....do....	.317	.199
Dry fiber.....do....	.159	.1147
Green fibrous waste.....do....	.273	
Dry fibrous waste.....do....	.199	.635
Percentage of dry waste per stalk	1.25	4.54
Percentage of dry fiber per stalk	1.00	.821

Explanation of results.—In order to explain the data recorded in the above table it is necessary to describe the manner in which the stalks were prepared for the two methods of treatment. For the hand stripping, about one foot of each end of the stalks was chopped off to facilitate the removal of the petioles, and three or four of the outer ones, which were bruised and discolored, were also discarded. Then, two or more ribbon-like strips were peeled from the entire length of the outer surface of each layer of the remaining portion of the stalk. Only these thin, fibrous ribbons were subjected to the stripping process. All the cellular portions of each petiole, together with the outer sheathes and the cut ends, were discarded. These constitute a class of waste distinct from that which results from the stripping operation itself. For reasons which will appear later, this waste is designated as *semifibrous* in distinction from the genuine *fibrous* material collected under the stripping knife.

In the case of the machine-stripped fiber, the stalks were prepared by first removing the ends and outer petioles, as in the method mentioned above, but the remainder was cut lengthwise into sections of the requisite width and then fed directly into the machine, without any attempt being made at the separation of the fibrous from the cellular portions. Hence, the 635 grams of dry waste which remained represented the quantity produced by the actual stripping process and must directly be compared with the 199 grams of dry, fibrous waste obtained by the other method. The machine removed so much water from the waste that its weight in a green state would have afforded no value for comparison; therefore it was not determined.[11]

The machine employed for this test was still in an experimental stage, hence the results obtained do not afford reliable data as to the possible

[11] Concerning the percentage of mercantile fiber produced by the two different methods of stripping, it will be observed that only 114 grams per stalk were obtained by machine stripping, as compared with 159 grams per stalk by hand stripping. However, it is only fair to state that the machine-stripped fiber was of better quality, being more polished and drier, as the comparative weights of green and dry fiber show.

effect of machine stripping on the future supply of abacá fiber and waste, but it was the only opportunity which has thus far presented itself for obtaining even approximate information in regard to this question. This machine waste contains a large amount of fiber of value to the paper maker and the quantity of waste demonstrates the fact that, whereas the outer surface of the leaf petioles undoubtedly contains the strongest fibers which are so valuable to the cordage maker, the cellular portion of the petioles also contains much fiber which is entirely lost by the hand-stripping process.

Semi-fibrous waste.—No determination of the percentage of the semi-fibrous waste, above referred to, was made at the time the stripping experiments were conducted. Later, an approximate determination of the amount produced by a given stalk was arrived at in the following manner: A complete stalk of abacá, weighing 15.876 kilos, was chopped into small pieces and subjected to hydraulic pressure. The dried residue weighed 1.592 kilos, so that the original stalks contained 10 per cent of vegetable matter and 90 per cent of water, calculated on the gross weight. In the case of the hand-stripped stalks only 2¼ per cent of these solids is accounted for. This loss of nearly 80 per cent, or four-fifths of the total solids of the stalk, caused us to collect and dry some of this waste material for a determination of its cellulose content. These and all subsequent digestion experiments were conducted on 1-kilo lots of dry material.

Experiment No. 1.—Strength of the caustic soda liquors, 2 per cent; 15 per cent of caustic soda calculated on dry weight of material treated; pressure, 6–8 atmospheres; time, 8 hours; yield, 33 per cent; digestion, incomplete; residue, brown and coarse and only fit for cheap, colored wrappings.

Experiment No. 2.—Strength of liquor, 3⅛ per cent; 25 per cent caustic soda calculated on dry weight of material; pressure, 6–8 atmospheres; time, 8 hours; yield, 20.5 per cent; apparently well digested; light-gray residue.

Experiment No. 3.—Strength of liquor, 5 per cent; 45.5 per cent caustic soda calculated on dry weight of material; other conditions same as above; yield, 20 per cent.

From the above results we see that this waste is semi-fibrous. The time required, the pressure, and the strength of the caustic soda necessary to remove the cellulose portions of this waste will undoubtedly prohibit its use. No further experimentation with this material was made. For the manufacture of wrapping paper, where color is not so important as is strength and cheapness, the waste could be lime-boiled under pressure, and but partially bleached, as is done with jute.

Fibrous waste.—The waste material, which results from the present method of extraction of the fiber for cordage and textile purposes, consists essentially of broken, tangled, but clean, fibers mixed with strips or bands of fiber aggregates, from which the cellular and incrusting matter has not entirely been removed. Its cellulose content varies, being of course dependent upon the amount of these soluble constituents which

are present. The readiness with which it is reduced to the condition of paper pulp, the kind and strength of chemicals required, and the time necessary for proper digestion likewise depend on this same factor. The fibrous waste was prepared for experimentation in much the same manner as old rope or rags are treated—namely, it was cut by hand into short pieces, thoroughly cleaned from all adhering sand and dirt and digested with caustic-soda liquor at elevated temperatures. The residues were drained and washed with hot water until they were free from alkali and the washings were colorless; they were then dried to constant weight in a water-jacketed air bath.

Experiment No. 1.—Strength of liquor, 2 per cent; 17 per cent caustic soda calculated on weight of material digested; pressure, 6–8 atmospheres; time, 4½ hours; yield, 36.65 per cent; residue, brown-gray in color, not entirely free from cellular matter.

Experiment No. 2.—Strength of liquor, 3½ per cent; 25 per cent caustic soda calculated on weight of material; pressure, 6–7 atmospheres; time, 4½ hours; yield, 32.84 per cent; well-cooked pulp of a light-gray color.

Experiment No. 3.—Strength of liquor, 3¾ per cent; 30 per cent caustic soda calculated on weight of material; pressure, 6–7 atmospheres; time, 5 hours; yield, 31.7 per cent.

Experiment No. 4.—Strength of liquor, 4⅜ per cent; 40 per cent caustic soda; other conditions same as No. 3; yield, 31.64 per cent.

Experiment No. 5.—Five per cent liquor; 45½ per cent caustic soda; other conditions same as above; yield, 31.51 per cent.

The waste employed in the above experiments was obtained from a machine-stripping process. Reference to the table on page 443 shows the relatively high percentage of dry machine waste as compared with the hand-stripped article. This explains the low cellulose content obtained. The experiments bring out the following points:

First. Two per cent liquor is insufficient with the pressure and time employed.

Second. Three and three-fourths per cent liquor is as efficient as the stronger concentrations.

Third. The gradual but constant lowering of the yield in experiments 3, 4, and 5 is due to the fact that the stronger liquors attack the cellulose, but pressures of 6–7 atmospheres may safely be employed because, under these conditions, the solvent action is very slight.

The conditions of time, pressure, and strength of caustic soda which give the best results are approximately one-half of those employed in the manufacture of wood pulp by the soda process.

A second series of five digestions was made on abacá waste resulting from the hand process of extracting the fiber. The preliminary preparation of the material was the same as in the preceding experiments. In each case a 3½ per cent caustic soda solution was employed, 25 per cent caustic calculated on the weight of the material digested. The pressure was held for five hours at 6 atmospheres as a minimum and 7 atmospheres as a maximum. The yields were 38.89, 41.69, 42.59, 42.66, and 42.14

per cent, respectively. The resulting pulps were of a light-gray color and devoid of the harsh feel which comes from insufficient cooking.

For purposes of comparison, two specimens of old Manila rope, representing the extremes of quality of such material for paper manufacture, were examined.

Preliminary treatment.—The pieces of rope were cut down and thoroughly cleaned and dusted as is the practice in mills where such material is used.

Specimen No. 1.—A good grade of 1-inch rope but badly frayed and worn; lost 21 per cent in cleaning.

Experiment No. 1.—Strength of liquor, 3⅛ per cent; 25 per cent caustic soda calculated on weight of material digested; boiled 5 hours at 6–8 atmospheres; yield, 61 per cent, equal to 48.7 per cent calculated on the original weight of rope.

Specimen No. 2.—A very dirty one-half inch rope of native manufacture, containing some unstripped strands of abacá; lost 21.82 per cent in cleaning.

Experiment No. 2.—All conditions of digestion same as above; yield, 43.89 per cent, equal to 34.31 per cent pulp, calculated on original weight of the rope.

Depletion of the land by removing abacá waste.—It is a fundamental principle of modern agriculture that all straw grown on a farm should be returned to the soil, and this applies to such by-products as cornstalks and sugar cane as well. The following analysis shows the comparatively low fertilizing value of abacá waste, so that its removal from the land in a dry state would not effect any appreciable loss of plant foods:

	Per cent.
Total nitrogen	0.52
Total phosphoric acid (P_2O_5)	0.046
Potash as K_2O	0.661
Lime (CaO)	0.238

It was shown on page 444 that 90 per cent of the green weight of an abacá stalk is represented by juice. This, on evaporation, was found to contain 2.62 per cent of solids or 275 grams from 15.876 kilos of stalk. A fertilizer analysis of this solid matter, obtained by evaporating the expressed liquid, was made by Mariano Vivencio, of this Bureau:

	Per cent.
Total nitrogen	0.40
Total phosphoric acid (P_2O_5)	1.86
Potash as K_2O	30.56

The presence of nearly 1 per cent of available potash in the juice is noteworthy because it shows the inorganic constituent needed by the growing plant and indicates the proper treatment for depleted abacá lands. Good wood ashes, the cheapest and best of potash fertilizers, contain on an average only 5 per cent of available potash. The juice from the stalks should therefore be returned to the land.

BLEACHING.

The operation of bleaching paper pulp as it is practiced under factory conditions, where time is the important factor, is difficult to approximate

in the laboratory. However, quantitative bleaching experiments allow of considerable accuracy and should afford fairly reliable data for comparative purposes under practical conditions.

Bleaching powder (chloride of lime) is used almost to the exclusion of all other agents, so that it alone need be considered. This chemical is usually applied in the form of a clear solution of approximately 5° Bé. strength (specific gravity, 1.036), made by disintegrating the powder in water and clearing it by allowing it to settle or by filtering. The amount of bleaching powder necessary to produce the required shade depends on several factors, chief among which is the completeness of the previous treatment—that is, the removal of the noncellulose.[12] The kind of fiber to be bleached also materially affects the amount of bleaching agent required. It is the practice to base all calculations as to quantity upon the amount of bleaching powder required to bleach 45.4 [13] kilos of the original fiber. The quantities in general use for this weight of different fibers are stated as follows:

	Kilos.[14]
Rags (cotton and linen fiber)	0.907– 2.268
Straw	3.175– 4.53
Esparto	4.53 – 6.80
Wood	5.44 –11.34
Jute and Manila	4.53 – 9.07

The pulp is bleached either in the beating machine or in large chests termed "plotchers." The exact procedure varies in the different mills, but time-saving devices and schemes are quite generally employed—that is, acid is added to hasten the bleaching action and artificial heat is supplied for the same reason. The following details of procedure, adopted for quantitative bleach experiments on abacá, apply as well to all the other fibers studied. It will be noted that all digestion experiments were performed on 1-kilo lots of raw material. This furnished in most instances about 450 grams of pulp. The washed, dry residues were repulped by beating or shaking with a definite volume of water, and a clear solution of bleaching powder of known strength was added, slightly in excess of the amount required to produce a good white. In some instances the operation was performed in a model beating engine of the Hollander type of about one-half kilo capacity, but most of the bleaching

[12] A well-boiled pulp should contain 90 to 95 per cent of cellulose—that is, will lose from 5 to 10 per cent in weight in the process of bleaching. Cross and Bevan: *Text-book on Paper Making*, 160.

[13] 100 pounds.

[14] 2– 5 pounds.
7–10 pounds.
10–15 pounds.
12–25 pounds.
10–20 pounds.

was done in 3-gallon glass jars provided with mechanical agitators. The experiments were conducted at ordinary temperatures (about 30° C.), and no attempt was made at "souring" by means of acids or of otherwise accelerating the action. The endeavor was rather to obtain a slow, regulated process which involved the least injury to the cellulose and a maximum yield of bleached pulp. After a good, white appearance was obtained to the beaten pulp, the stuff was filtered and the residual available chlorine determined by titrating an aliquot portion of the filtrate with a standard solution of thiosulphate. The filtering and washing of the bleached cellulose was performed by means of suction, a large Buchner funnel with small perforations, proving a very efficient mold in which to wash and press the pulp into discs for a final weighing.

BLEACHING ABACÁ PULP.

Experiment No. 1.—The dry residue from digestion No. 2, page 445, amounting to 328.4 grams, was placed in the engine and beaten to a homogeneous mass with 9 liters of water, then 2½ liters of clear bleaching powder solution, strength 2.35 per cent available chlorine (approximately 10° Bé.) were run in and the stirring continued until the pulp was of a light cream color. At this stage 100 cubic centimeters of the liquor required 31 cubic centimeters of N/10 thiosulphate, equivalent to 0.11 gram of chlorine, or to 12.1 grams of residual chlorine in the entire liquor. The amount of chlorine added (2½ liters of 2.35 per cent chlorine solution) was 58.75 grams. The difference between this quantity and the 12.1 grams remaining at the end of the bleach, amounting to 46.65 grams, represents the amount used in bleaching 324.8 grams of pulp or 1,000 grams of original waste. This is 14.2 per cent of chlorine, calculated on the weight of pulp, or 4.66 per cent calculated on the weight of the raw material originally taken. Using bleaching powder of 35 per cent available chlorine as a basis for calculating into terms of general usage, the above results are equivalent to 14.2 per cent of powder.[15] The dry, bleached residue weighed 304.4 grams, so that there was a loss of 7.3 per cent in the bleaching operation.

Experiment No. 2.—The residue from digestion No. 3, page 445, weighing 317 grams was employed. A bleach liquor of much less strength (1.65 per cent available chlorine, approximately 3½° Bé.) was used, otherwise the conditions were the same as in the preceding experiment. The amount of bleaching powder required was 12.22[16] per cent of the raw material. The dry bleached residue weighed 297 grams, so that there was a loss of 6.4 per cent in bleaching.

CHEMICAL INVESTIGATION OF FIBROUS SUBSTANCES IN GENERAL.

The schemes which have been used for the analysis of fibrous substances and the methods adopted for valuing unknown raw materials for paper stock are substantially those of Messrs. Cross, Bevan, and King, whose valuable works on fibers,[17] cellulose,[18] and paper making[19] stand

[15] 13.33 pounds per hundredweight of waste.

[16] 12.2 pounds per hundredweight of waste.

[17] *Indian Fibers and Fibrous Substances* (1887), London, Spon, E. and F. N.

[18] *Cellulose* (1895), London, Longmans, Green & Co.

[19] *Paper Making* (1900), London, E. & F. N. Spon.

preëminent in this interesting field of chemical research. The principal scheme of analysis used by these chemists is briefly, as follows:

	Moisture	Hygroscopic water, or water of condition. Loss on drying at 100° C.
Separate portion taken for each determination. (Results calculated in percentage of dry substance.)	Ash	Total residue left on ignition.
	Hydrolysis (*a*)	Loss of weight on boiling raw fiber five minutes in 1 per cent solution of caustic soda.
	Hydrolysis (*b*)	Loss of weight on continuing to boil one hour.
	Cellulose	White or bleached residue from following treatment: (1) Boiling in 1 per cent solution of caustic soda five minutes; (2) exposing to chlorine gas one hour; (3) boiling in basic sodium sulphite, 2 per cent solution.
	Mercerizing	Loss on treating one hour with 33 per cent solution of caustic soda, cold.
	Nitration	Weight of nitrated product obtained by treatment with a mixture of equal volumes of nitric and sulphuric acids one hour in the cold.
	Acid purification	Raw fiber boiled one minute with acetic acid (20 per cent) washed with alcohol and dried.
	Carbon percentage	Determined by combustion.

This method of study is of value in that it gives results which are dependent upon definite properties of the fiber substance, but it is more extended than is required for special or more practical purposes, therefore it has been restricted to our wants and also modified in some respects.

Moisture.—As is well known, all celluloses under normal conditions contain a certain amount of moisture which is termed "water of condition," which is quite definite for each fiber, although it varies within limits which are dependent upon the hygrometric state of the atmosphere. It is characteristic of abacá waste that it readily absorbs moisture and in an ordinarily dry condition holds from 11 to 13 per cent, but during the rainy months the water content was found to reach a maximum of 18 per cent. This hygroscopic moisture is a factor of some importance in the buying and selling of fibrous substances either in the raw state or as paper pulp. It is customary to decide on some arbitrary percentage as representing the moisture normally present. The standard used varies with different countries and with different kinds of material. With wood-pulp, in which there is considerable commerce, 10 per cent is usually taken as representing the moisture normally present.

Graffin and Little[20] give the following method for calculating the percentage of air-dry material: A representative sample of the substance to be tested is dried in a water-jacketed air bath at 100° to constant weight. The loss in weight represents the moisture in the sample and is calculated into percentage, the difference between this figure and 100 giving the percentage of absolutely dry fiber. On a 10 per cent basis every 90 parts by weight of dry material is equivalent to 100 parts of air-dry substance; on this basis, dividing the percentage of dried material formed by 90 and multiplying the quotient by 100 gives the percentage of air-dry substance.

Example: A sample of waste lost 15 per cent on drying, then 85 per cent represents the dried fiber; if the standard is 10 per cent, then $85/90 \times 100 = 94.4$ per cent,[21] or the percentage of air-dry fiber actually in the amount of material paid for on a 10 per cent basis.

The effect of this water of condition on commercial dealings in fibrous products is emphasized when values are considered. In the delivery of, say, 2,272.7 kilos of material at 4.4 cents per kilo,[22] the difference is 127.2 kilos or $5.60.

Ash.—"The ash in isolated fibers is low, viz, 1–2 per cent; in fiber aggregates it is often high—thus, in esparto and straw from 3 to 6 per cent—and should be taken into account in calculation of yields or loss of weight." [23]

I have found several samples of rice straw to average 18 per cent of mineral matter; but this is an extreme case. Griffin and Little give the range from 3 to 7 per cent, or in exceptional cases as high as 12 per cent on the dry straw, and further add that the strongest straw yields the most ash.

Alkaline hydrolysis.—"This is obviously the first stage toward the isolation of cellulose. When the numbers obtained for the short period (*a*) and for the long digestion (*b*) show a marked difference, it is an obvious general indication of low paper-making quality." [24]

Cellulose.—Cross and Bevan's chlorination method gives the maximum theoretical yield. Various other available methods give figures which are 2 to 5 per cent lower, but in comparison they consume much time. All the cellulose determinations recorded in this paper have been made on the residue from hydrolysis (*b*) which yields results more nearly in accord with other methods, at the same time avoiding their tediousness. After this preliminary discussion of methods and their meaning, the results of the chemical investigation of abacá fiber will be given.

[20] *Chemistry of Paper Making*, 451.
[21] 94.4 pounds of normal, air-dry fiber per hundredweight.
[22] 2½ tons at 2 cents per pound.
[23] Cross and Bevan: *Text book of Paper Making*, p. 92.
[24] *Loc. cit.*

CHEMICAL INVESTIGATION OF ABACÁ FIBER.

Ash, alkaline hydrolysis, and cellulose calculated on dry weight.

	Per cent.
Moisture	8.10
Ash	1.08
Hydrolysis (*a*)	13.86
Hydrolysis (*b*)	20.79
Cellulose	73.68

Composition of raw abacá fiber (undoubtedly hand stripped).

[Analysis by Hugo Müller.[25]]

	Per cent.
Cellulose	64.07
Fat and wax	.62
Aqueous extract	.96
Lignin and pectous substances	21.60
Water	11.73
Ash	1.02

Figures obtained by myself on a sample of machine-stripped fiber.

	Per cent.
Cellulose	63.15
Fat and wax	.66
Aqueous extract	1.00
Lignin and pectous substances	24.67
Water	9.50
Ash	1.02

MICROSCOPIC CHARACTERISTICS OF ABACÁ FIBER.

Manufacturers of paper attach considerable importance to the physical condition of cellulose after it has been freed from foreign matter and otherwise purified by the boiling, washing, and bleaching processes to which it has been subjected.

Some fibers are short, hard, and of polished exterior, while others are long, flexible, and barbed; the former, it is scarcely necessary to say, yield but indifferent papers, easily broken and torn, while papers produced by the latter class of fibers are possessed of a great degree of strength and flexibility.[26]

According to Watt:[27]

Straw fiber is short, pointed and polished, and can not of itself make a strong paper; on the other hand, Manila (abacá) is the strongest known, and esparto fiber holds an intermediate place between these two extremes.

The dimensions of abacá fiber are included in the table given on page 461, together with those of the others examined. For purposes of

[25] Griffin and Little: *Chemistry of Paper Making*, p. 127.
[26] Arnot: *Journ. Soc. Arts*, 26, 74.
[27] *Art of Paper Making* (1901), p. 4, Crosby, Lockwood & Son, London.

comparison the measurements of many well-known commercial fibers are also given.

The microphotographs depict the fibers both in transverse and longitudinal sections. The relative widths of the fiber walls and central canals as well as their rounded or polygonal forms and the shape of the tips, are clearly illustrated.

DIRT AND FOREIGN MATTER IN ABACÁ WASTE.

The cleanness of the raw material is an important consideration with paper makers. Foreign substances, such as sand, do not disappear in the pulping process and appear to be multiplied in the bleached and beaten half stuff.

In this respect abacá waste as it is ordinarily collected becomes very much contaminated. The greater part of this accumulation of foreign matter can be avoided if extra care is taken in the stripping of the fibers, but even then the waste would need to be thoroughly dusted at the factory and either picked over by hand or cleaned by machinery, according to the methods used for the preparation of dirty rags and rope.

The Philippine Islands are the home of real Manila paper stock. The qualities which give to abacá its prominent position among the fibers of the world—*i.* e., its strength and durability—make it a source of paper stock par excellence. The same conditions which confront paper manufacturers in other parts of the world are to be met here. The material must be collected from widely scattered localities, but with improved means of transportation it seems possible that this waste from abacá could be baled and shipped to market along with the cordage fiber. This will soon be the case when it becomes generally known that a product which has hitherto been a total loss will command from 1 to 2 cents a pound and the result will be to augment the revenues of the Manila hemp industry by millions of dollars annually.

PLANTAINS AND BANANAS.

Two other species of the family of plants to which abacá belongs, namely, the banana (*Musa sapientum*) and plantain (*Musa paradisiaca*), are worth considering in regard to their availability for paper stock. The Philippines and the Indian Archipelago are regarded as the regions richest in bananas.

> This highly important fruit grows in every province and inhabited island of the Philippines, both in the wild and cultivated state, and numbers over fifty species. The statistics regarding its production and area are interesting only as indicating the extent to which the natural, spontaneous growth has been supplemented and added to by such industry as the natives have exerted in setting out plants in the vicinity of their houses, which after planting receive very little, if any, attention in the way of real cultivation.[28]

[28] *Report of the Philippine Census* (1905), 4.

The entire cultivated area devoted to bananas in the Archipelago was reported as being 33,913 hectares (83,802 acres), upon which 14,078,600 bunches of the fruit were said to have been produced. This also represents the number of stalks which practically go to waste at the present time, for, after the fruit is harvested, they are simply allowed to rot on the ground. These data do not include the wild, nonedible species of plantains which are so common in all parts of the Islands.

Dr. Forbes Royle [29] in discussing plaintains says:

> Of the value of plantain fiber for paper making, there can, I conceive, be no doubt. Some paper, though unbleached, but excellent as far as substance and tenacity are concerned, was sent from India by Dr. Hunter in 1851. In 1846 Mr. May showed the author some beautiful specimens of note and letter paper made from plantain fiber. Mr. Routledge subsequently made some excellent paper, both of a tough and of a fine quality, from fibers of this species of Musa.

The Bulletin of the Royal Kew Gardens for August, 1894, contains a valuable summary of information relating to bananas and plantains from which the following brief extracts have been taken:

> In Jamaica a series of experiments, undertaken by Mr. Morris in 1884, showed that the plantain fiber (*Musa sapientum* var. *paradisiaca*) was whiter and finer than ordinary banana fiber and that it approached more nearly the fine, glossy character of Manila hemp. A banana stem weighing 108 pounds yielded 25 ounces of cleaned fiber, or at the rate of 1.44 per cent of the gross weight. A plantain stem weighing 25 pounds yielded 7¼ ounces of cleaned fiber, or 1.81 per cent of the gross weight.
>
> The experiments of ten years on a cultivation of from 400 to 480 acres in plantains has shown that, first, 700 to 800 stems are cut per acre per annum, either for fruit or in consequence of having been blown down by high winds or from disease or other reasons; second, if planted 8 feet apart and cut every eight months for stems alone an acre would give 1,400 to 1,500 stems each cutting, or about 4,500 in two years; third, plantain stems average 2½ pounds of clean and 1½ pounds discolored and broken fiber, the latter only fit for coarse paper. These results, however, were obtained with very imperfect machinery; fourth, the average weight of a plantain stem is 80 pounds.

Complete stalks of wild plantain from Tarlac Province, Philippine Islands, were found to average over 100 pounds in weight. One entire stalk was sawed into short cross sections and subjected to strong pressure. The dried residue was 9.3 per cent of the gross weight of the stem. Crude fiber estimation (Weende Method) gave 2.46 per cent of the gross weight of the stem. A second stalk was divided longitudinally into narrow strips. These were drawn under a knife edge, which removed the greater proportion of the water and cellular matter. The remaining thin, fibrous ribbons were boiled in a dilute solution of sodium carbonate containing a proportionate quantity of quicklime until the

[29] Royle: *The Fibrous Plants of India*, p. 87

incrusting substances were dissolved. Thorough washing produced 1 kilo of light-gray textile fiber.

The following data are reported by Mariano Vivencio, of this Bureau:

Comparison of a stalk from an edible variety of banana with one from abacá.

	CRUDE FIBER.	WATER.
	Per cent.	Per cent.
Banana stalk (green)	2.21	91.48
Abacá stalk (green)	2.90	92.70

PULPING AND BLEACHING EXPERIMENTS ON STRIPPED AND UNSTRIPPED PLANTAIN FIBER.

Experiment No. 1.—Six hundred and eighty grams of the cleaned fiber, obtained by boiling the outer fibrous strips of plantain stalks in dilute sodium carbonate and lime (see p. 453) were digested under 5–6 atmospheres pressure for five hours, with 20 per cent caustic soda, calculated on the weight of the material. The washed, dry residue weighed 442 grams, equal to a yield of 65 per cent. This residue was repulped in an excess of water and bleached under exactly the same conditions as those used for bleaching abacá pulp. Chlorine consumed, 15.2 grams, equivalent to 43.4 grams of bleaching powder of 35 per cent strength.[30] The dry, bleached pulp weighed 404 grams, a loss of 8.6 per cent in bleaching.

The plantain fiber when it is extracted is of a white, silvery luster and contains many strong filaments. However, in this respect it is very inferior to abacá. This inferiority for cordage purposes proves to be an advantage when it is considered for paper stock, for the ease of resolution into the ultimate fibers is directly proportional to the tensile strength of the filaments.

CHEMICAL INVESTIGATION OF PLANTAIN FIBER.

Ash, alkaline hydrolysis, and cellulose calculated on dry weight.

	Per cent.
Moisture	10.02
Ash	3.46
Hydrolysis (*a*)	16.78
Hydrolysis (*b*)	27.42
Cellulose	68.21

Composition of raw fiber from plantain.

	Per cent.
Cellulose	61.68
Fat and wax	1.06
Aqueous extract	1.77
Lignin and pectous substances	22.79
Water	9.57
Ash	3.46

[30] 9.81 pounds of powder per hundredweight of pulp, 6.38 pounds of powder per hundredweight of raw fiber.

MAGUEY.

Agave cantula.

After abacá, maguey or sisal hemp may well be ranked as the second most important fiber-producing plant of the Philippine Islands. The maguey plant is widely distributed throughout the Archipelago and has long been used for local purposes.[31]

The structural fiber of this and of other species of *Agave* is used for cordage and like abacá, it finds its way to the paper mills in the form of old rope, binder twine, etc. The following figures were obtained on a specimen of machine-stripped maguey fiber:

Ash, alkaline hydrolysis, and cellulose calculated on dry weight.

	Per cent.
Moisture	9.23
Ash	1.96
Hydrolysis (*a*)	13.78
Hydrolysis (*b*)	15.70
Cellulose	77.05

The corresponding data on *Agave keratta* from the West Indies, given by Cross, are:

	Per cent.
Moisture	15.5
Ash	1.4
Hydrolysis (*a*)	10
Hydrolysis (*b*)	20
Cellulose	75.8

Composition of the raw fiber.

	Per cent.
Cellulose	70.09
Fat and wax	.71
Aqueous extract	1.54
Lignin and pectous substances	16.84
Water	9.03
Ash	1.79

MAGUEY WASTE.

The waste fiber employed for the following digestion experiments was taken during some machine-stripping tests which were made on maguey leaves from Vigan, Ilocos Sur, by the Bureau of Agriculture of the Philippine Islands. The possibility of materially reducing the weight and bulk of this waste material by boiling it with lime in the localities where it is produced suggested itself, and experiments to decide this question were first undertaken.

Experiment No. 1.—One kilo of partially cleaned, dry waste was boiled in an open kettle for twelve hours with 20 per cent of quicklime calculated on the weight of the material. The washed, dry residue weighed 685 grams, or 68.5

[31] *Report of the Bureau of Agriculture* (1904), 82.

per cent. The residue was unpulped, of a dark-brown color, and very coarse. Digested for five hours longer, under 6–7 atmospheres pressure with 10 per cent caustic soda calculated on the original weight taken. The yield was 31.5 per cent of a light-gray, well digested pulp.

Experiment No. 2.—Uncleaned waste; 20 per cent quicklime; time of digestion, five hours; pressure, 6–7 atmospheres; yield, 55 per cent of a coarse, brown residue only suitable for cheap wrapping paper.

Experiment No. 3.—Time of digestion, twelve hours; all other conditions as in experiment 2; yield, 38 per cent. The residue appeared to be well pulped, but not entirely free from cellular matter.

Experiment No. 4.—Twenty-five per cent caustic soda, calculated on the weight of material digested; time, five hours; pressure, 7 atmospheres; yield, 35 per cent; residue, light-gray, and it appeared to be very well boiled.

Experiment No. 5.—Twenty per cent caustic soda; time, five hours; pressure, 7 atmospheres; yield, 41.5 per cent; residue, dark-gray; digestion, incomplete.

Experiment No. 6.—Twenty per cent caustic soda; boiled twenty-four hours at ordinary pressure with reflux; yield, 50 per cent; residue similar to that from experiment 2.

Conclusions.—For the preparation of half stuff for brown wrapping paper the waste may be lime boiled under pressure with good results both in respect to yield and to economy; however, an open cook with lime gave negative results. The weight of the waste may be reduced by about 30 per cent by this latter procedure, but the resulting product is not in any sense a paper pulp. Caustic soda (25 per cent calculated on the gross weight of the material) effects a complete re-solution of the incrusting material.

BOWSTRING HEMP.

Sanseveria zeylanica is found quite widely distributed throughout the Islands and is cultivated in some localities for cordage and textile purposes. It is mentioned in this place because of the similarity which its structural fiber has to that of maguey and because of the possibility of its becoming a plant of considerable commercial importance. Like maguey, it readily lends itself to machine stripping and in the event of a more extensive cultivation the waste fiber may be worth considering.

GRASSES IN GENERAL.

Gramineæ.—Among the *Gramineæ* are many well-known annual and perennial plants which have in the past, largely been used in the manufacture of paper; the cereal straws, such as those of wheat, rye, oats, and barley, and the stalks of maize and of sorghum, are examples of materials from annual plants which are used for this purpose. Esparto and the British Indian grasses *Munj* and *Bhabur* may be mentioned among the perennial plants, as they have assumed a considerable commercial importance. The various species of bamboo have not as yet, because of the reasons stated on page 434, been industrially established.

Esparto.—The Esparto grass (*Stipa tenacissima*) is found both cultivated and in the wild state in the countries bordering on the Mediter-

ranean, principally in Spain and in northern Africa. In the regions where this grass grows the material is used for the manufacture of cordage, sandals, tie material, and basket work, but its great commercial importance lies in its use for paper stock. The cost of its production and of its shipment have excluded the use of esparto in the United States, where wood pulp has been so cheap and plentiful, but in Great Britain it has found a steady market, approximately 200,000 tons, valued at from $15 to $20 per ton, being imported annually into that country.

Bhabur grass.—The Bhabur grass (*Ischaemum augustifolium*) which is met with throughout the central table lands of India from Bengal to Madras, the northwest provinces and central India, is in some parts extremely abundant. As a paper material this grass has been reported as little inferior to esparto and the paper made from it is of good quality. The Indian paper mills use Bhabur grass largely.[31]

The Munj grass (*Saccharum sara*), which is common from Bengal to north India, as well as several other species of *Saccharum*, are largely used in the upper India mills near Lucknow. Indeed, this is one of the most valuable of Indian fiber materials, in some respects being superior to Bhabur grass. The great obstacle to its further use is the difficulty of procuring a large and constant supply.[32]

The following statistics which refer to the paper industry of India are especially significant in their bearing on the possibilities of paper production in the Philippines, as the raw materials in general use in the mills of India are very similar to those which we are about to discuss:

There are eight paper mills in operation, two of which are private concerns. The capital invested so far as information is obtainable is rupees 7,320,000 (approximately $2,500,000). Most of the white and blue foolscap and much of the blotting paper, note paper, and envelopes used in the Government offices are now made in the Indian mills.

The total quantity of paper made in 1902 was 47,000,000 pounds, valued at $2,092,000, approximately.

The capital has trebled in twenty years since 1883 and the production and number of persons employed has increased sixfold during the same period.[33]

PHILIPPINE GRASSES.

Cogon.—Two grasses, Cogon and Talâhib, are found in the Philippine Islands growing wild and apparently in sufficient quantities to warrant some inquiry as to their economic use. In the Philippines many coarse grasses are termed cogon, but, properly speaking, Cogon (*Imperata exaltata* Brong.) is the broad-leaved, gregarious variety, 2 to 4 feet in height, which grows in even stands on open lands, foothills, and mountains. Where nipa is not to be obtained the true cogon is highly prized for thatching purposes. Conditions of drought do not appear to affect

[31] Watt: *Dictionary of Economic Products of India*, 6, part 1.
[32] *Ibid.*
[33] *Indian Forester* (1904), 29, 482.

its growth, as it seems to thrive on a soil containing but little moisture; indeed, even in the driest season it will spring up in a green and thrifty manner after being burned over, while, on the other hand, it is not found along river bottoms or on lands subjected to overflow during the rainy season. The study of cogon grass was conducted in conjunction with that of esparto in this laboratory because the use to which it is proposed to put the former is identical with that established for the latter. A direct comparison is therefore important and necessary. We were furnished with the Spanish variety of esparto from Barcelona through the kindness of Don Enrique Zobel, of Manila, and of the Compañía General de Tabacos de Filipinas. Our thanks are due for the great courtesy.

Ash, alkaline hydrolysis, and cellulose calculated on dry material.

	COGON GRASS.	ESPARTO GRASS (SPANISH).
	Per cent.	Per cent.
Moisture	9.32	8.68
Ash	4.53	3.71
Hydrolysis (*a*)	25.77	19.75
Hydrolysis (*b*)	40.00	37.16
Cellulose	50.11	55.16

Chemical composition of cogon and esparto grass.

	COGON.	ESPARTO.
	Per cent.	Per cent.
Cellulose	46.68	48.25
Fat and wax	1.16	2.07
Aqueous extract	10.80	10.19
Pectous substances	26	26.39
Water	11.33	9.38
Ash	4.03	3.72

Experimental work with mature cogon grass, the results of which are given below, indicates, first, the yield of paper cellulose to be expected under factory conditions of treatment; second, the approximate amount of caustic soda necessary to produce a well-boiled pulp; third, the comparative, resistant nature of the cellulose to further hydrolysis.[35]

Percentage of—	Experiment 1.	Experiment 2.	Experiment 3.	Experiment 4.
Soda liquor	2	2.4	2.5	3
Caustic calculated on weight of material	10	12	12.5	15
Yield of pulp	47.34	45.5	45.42	44.25

[35] Well-dusted grass, free from weeds and root ends, was cut into pieces 2 to 3 inches long and in this condition placed into the autoclave. Dilute caustic-soda solution in amount sufficient to cover the grass was then run in and the pressure was rapidly raised to 4 atmospheres as a maximum. One kilo of dry grass was taken for each digestion; the duration of the boiling was six hours.

All four of the pulps were light-gray in color and they appeared to be well reduced. The digestions were carried out in an autoclave built of bronze and the heating was done with direct fire. By the use of patent boilers of the vomiting type and by heating with direct steam (improvements which are in general use with esparto grass) results equal to those given above could no doubt be brought about in a much shorter time. The pulp has a great tendency to form little balls which are very similar to those encountered with esparto and straw, hence rotary boilers would not be suitable. The modern tendency is either to increase the pressure or the amount of caustic soda used, thus diminishing the duration of the digestion.

Two digestions with 2 per cent liquor, but with 20 per cent caustic soda, calculated on the weight of the material, were carried out at 4 to 5 atmospheres pressure for three hours. The yields of pulp were 44 and 45 per cent, respectively.

In some cases, esparto and straw are boiled in open kettles, but if this is done, a much longer time is required to accomplish the same result. The following table gives the results of two such experiments:

Digestion of cogon at ordinary pressures.

	I.	II.
Strength of liquor (per cent)	2.6	3
Caustic soda (per cent)	13	15
Time of boiling (hours)	12	12
Yield of pulp (per cent)	51.25	48.81

These results show that cogon could be boiled in open digesters with good results, to make the cheaper grades of printing paper, where time is not as important a factor as the cost of the process. The use of quicklime, the chemical so commonly employed in the manufacture of strawboard, did not give satisfactory results with cogon grass because the lime seems to combine with the soluble constituents from the grass and it then becomes extremely difficult to wash out. The pulps produced in this manner in the laboratory were coarse and brown. However, for the cheapest printing paper and for boards, a lime boiling in an open cook, or perhaps under 1 to 3 atmospheres pressure, would effect great saving in the cost of the chemicals to be used.

The investigation of cogon also proved that no preliminary cutting down of the grass is necessary; after being dried and hand picked or machine cleaned it is fit for immediate digestion.

THE BLEACHING OF COGON GRASS PULP.

Experiment No. 1.—The residue from digestion No. 3, page 458, amounting to 454.2 grams, was repulped in 10 liters of water; 1 liter of a bleaching solution of 2.35 per cent available chlorine (approximately 10° Bé.) was added and the

whole allowed to bleach over night. No residual chlorine remained, but the pulp was of a clear, white color. The amount of chlorine consumed was 23.5 grams (1,000 cubic centimeters of 2.35 per cent solution). This represents 67.1 grams of powder, equivalent to 6.71 per cent.[36] The bleached pulp weighed 428.7 grams, which gave a loss of 5.62 per cent in bleaching.

Experiment No. 2.—A residue from digestion with 20 per cent caustic soda, page 459, amounting to 440 grams, was submitted to exactly the same conditions as those given above. The residual chlorine amounted to 0.78 gram, which leaves 22.72 grams as the amount consumed. This represents 64.9 grams of powder.[37] The bleached pulp weighed 418 grams which represents a loss of 5 per cent in bleaching.

TALÁHIB, Tag., *Lidda,* Ilo., *Tigbao,* Vis. (*Saccharum spontaneum*).

This is a coarse-jointed grass, 6 to 10 feet in height, gregarious, growing in tufts from stout underground rootstalks. It is found to be distributed from British India to southern China, Malasia, New Guinea, the Philippine and Caroline Islands. It is very common throughout the Archipelago and is frequently confounded with cogon grass, but it is very distinct from the latter in appearance and in its habit of growth. It thrives best in valleys and in low, moist places, especially in areas which are flooded during the rainy season. It is very persistent and difficult to eradicate; simple cutting or burning does not appear to decrease its growth but rather to improve its yield and quality. Other related species are *Saccharum sara* (the Munj grass of India) and *Saccharum officinarum* (the well-known sugar cane of all tropical countries). A sample of mature grass consisting of entire stems and leaves gave the following figures:

	Per cent.
Moisture	10.23
Ash	5.46
Hydrolysis (*a*)	27.44
Hydrolysis (*b*)	40.53
Cellulose	53.90

If this grass is allowed to become too dry before cutting, the nodes harden and prove difficult to pulp, and a considerable quantity of shive is the result, so that some mechanical crushing or breaking of the stems is necessary. Only one digestion experiment was made. The grass was cut into short pieces and boiled in water for three hours to soften the nodes, then digested during six hours with 12½ per cent of caustic soda, calculated on the weight of the grass. Pressure, 4 to 5 atmospheres. Yield of pulp was 45.57 per cent. The residue bleached to a good white with only 3.2 per cent loss in weight by the use of 5.7 per cent of bleaching powder, calculated on the original weight of the material digested.

[36] 6.71 pounds of bleaching powder per hundredweight of grass.
[37] 6.43 pounds of bleaching powder per hundredweight of grass.

DIMENSIONS OF THE ULTIMATE FIBERS OF SOME PHILIPPINE FIBER PLANTS.

[Table by Dr. E. B. Copeland. All measurements are in millimeters.]

Name.	Length.			Diameter.					
				Total.			Lumen.		
	Maximum.	Average.	Minimum.	Maximum.	Average.	Minimum.	Maximum.	Average.	Minimum.
Abacá (*Musa textilis*)	6.00	3.98	2.45	0.021	0.017	-------	0.009	0.0066	-------
Plantain (*Musa sapientum* var. *paradisiaca*)	7.30	5.49	4.15	.026	.020	0.018	.016	.0106	0.007
Maguey (*Agave cantula*)	4.93	2.38	1.00	.026	.018	.015	.013	.007	.004
Cogon grass (*Imperata exaltata*)	1.82	0.99	0.46	.021	.011	.005	.013	.0044	.001
Taláhib grass (*Saccharum spontaneum*)	2.82	1.59	0.80	.020	.015	.012	.010	.0043	.1115
Bamboo (*Bambusa blumeana*)	-------	1.81	-------	-------	.0075	-------	-------	-------	-------
Dwarf bamboo (*Bambusa lumanpao*)	4.10	2.57	1.20	.028	.0156	.005	.025	.018	.001
Rice straw (*Oryza sativa*)	-------	0.88	-------	-------	.0025	-------	-------	-------	-------
Buri palm (*Corypha umbraculifera*)	2.80	2.11	1.10	.015	.013	.010	.007	.0034	.002

Table of dimensions of some of the more important fibers used in the manufacture of textiles and paper.

[Taken from M. Vetillart.[38]]

Name.	Length of fiber cell.			Diameter of fiber cell.		
	Maximum.	Mean.	Minimum.	Maximum.	Mean.	Minimum.
Flax (*Linum usitatissimum*)	66.0	25–30.0	4.0	0.037	0.022	0.015
Hemp (*Cannabis sativa*)	55.0	22.0	5.0	.050	.022	.016
Jute (*Corchorus olitorius*)	5.0	2.0	1.3	.025	.020	.020
Esparto grass (*Stipa tenacissima*)	3.5	0.5	1.3	.018	.0125	.007
Spanish grass (*Lygeum spartum*)	4.5	2.5	1.3	.020	.016	.012
Bowstring hemp (*Sanseveria* sp.)	6.0	3.0	1.5	.026	.020	.015
Paper mulberry (*Broussonetia papyrifera*)	25.0	15.0	6.0	.035	.030	.025
Talipot palm (*Corypha umbraculifera*)	5.0	3.0	1.5	.028	.024	.016
Coconut palm (*Cocos nucifera*)	1.0	7.0	0.4	.024	.020	.012

We are greatly indebted to Mr. Elmer D. Merrill, Botanist of the Bureau of Science, for the collection and botanical identification of fibrous plants discussed in this paper and for other valuable assistance.

[38] *Etudes sur les Fibres Vegetales Textiles.*

EXPLANATORY NOTE ON THE SPECIMENS OF PAPER INSERTED IN THIS ARTICLE.

In response to numerous requests for specimens of paper made from the raw materials investigated, we have inserted into this number of the JOURNAL samples of handmade paper from abacá waste and cogon grass. Similar specimen sheets made from banana, bamboo, palms, and other material will be sent on request. It was thought best not to alter the pulp in any way, but only to provide pure bleached specimens, thus affording paper manufacturers and others who are interested an opportunity for testing the fiber to their own satisfaction. Consequently, no attempt at loading, sizing, coloring, or calendering the specimens was made. The work required to turn out several reams of handmade paper with apparatus available in the laboratory is very great, and it was practically all performed by Filipinos. This speaks favorably for their skill in acquiring facility in manipulations of this kind.

In a future paper other Philippine paper materials will be discussed, and data in regard to the available supply of all raw materials, so far as such data can be obtained, will be given.

ILLUSTRATIONS.

[Photomicrographs by Martin.]

PLATE I.

ABACÁ (*Musa textilis*).

FIG. 1. Transverse section of isolated fibers.
2. Fibers seen longitudinally.

PLATE II.

PLANTAIN (*Musa paradisiaca*).

FIG. 1. Transverse section of group of fibers.
2. Fibers seen longitudinally.

PLATE III.

MAGUEY (*Agave cantula*).

FIG. 1. Transverse section of a group of fibers.
2. Fibers seen longitudinally.

PLATE IV.

COGON (*Imperata exaltata*).

FIG. 1. Transverse section of a bundle of fibers.
2. Fibers seen longitudinally.

PLATE V.

TALÁHIB (*Sacharum spontaneum*).

FIG. 1. Transverse section of isolated fibers.
2. Fibers seen longitudinally.

PLATE VI.

ESPARTO (*Stipa tenacissima*).

FIG. 1. Transverse section of isolated fibers.
2. Fibers seen longitudinally.

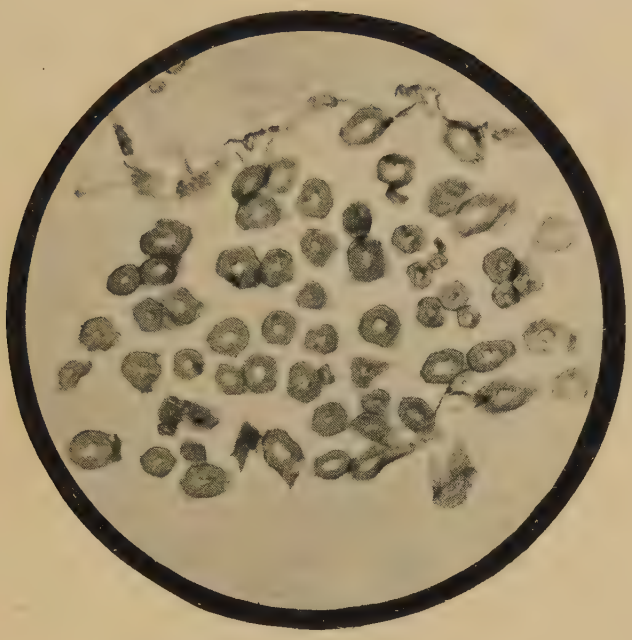


FIG. 1.

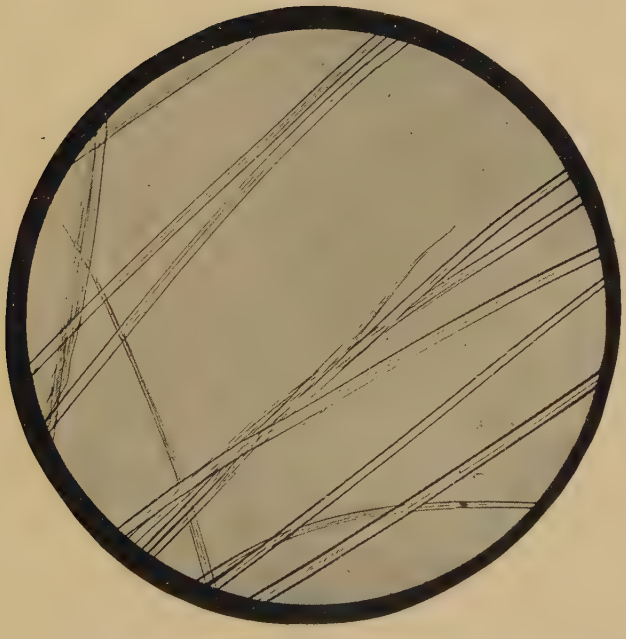


FIG. 2.

PLATE I.

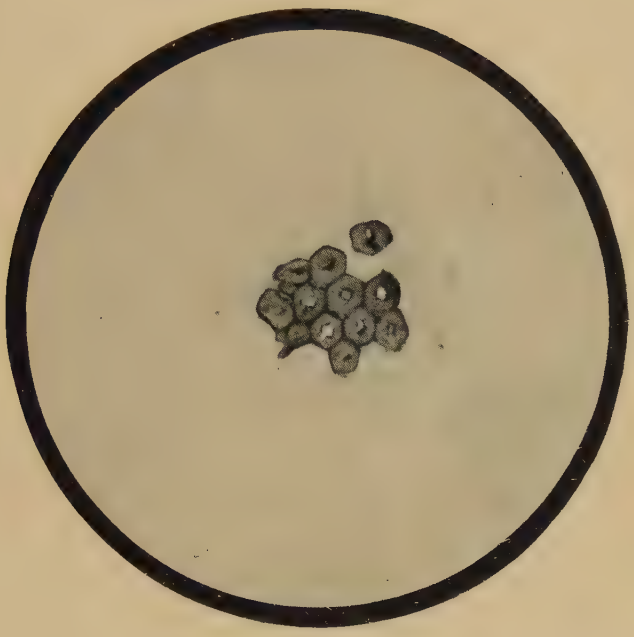


FIG. 1.

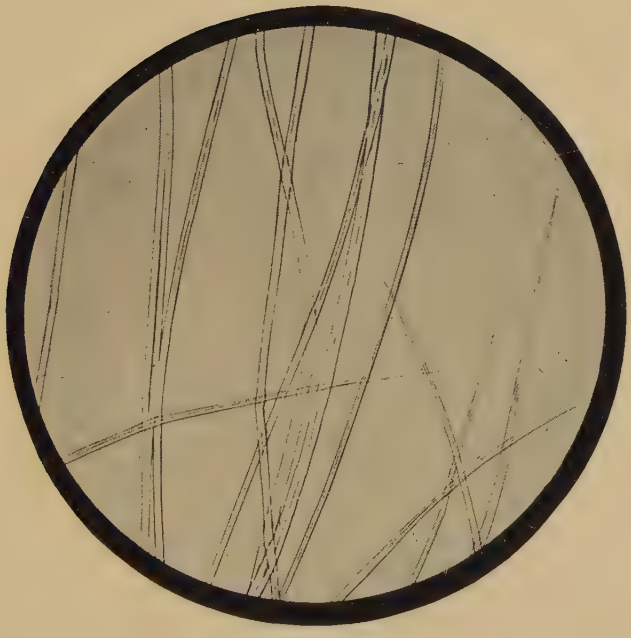


FIG. 2.

PLATE II.

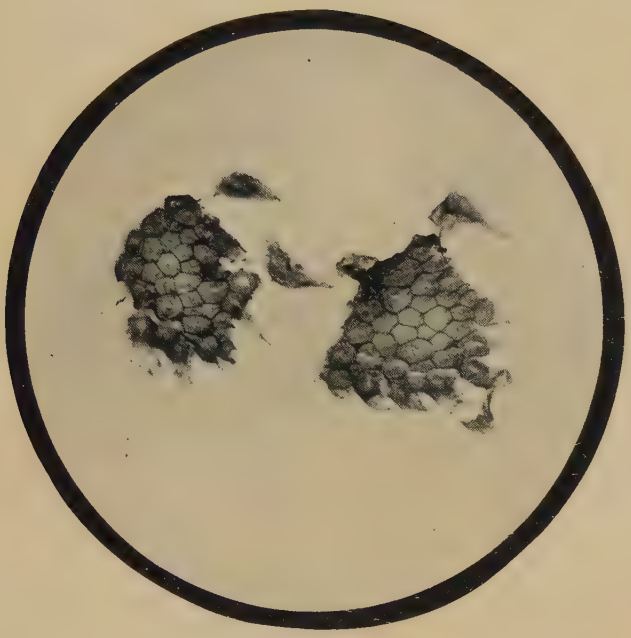


FIG. 1.

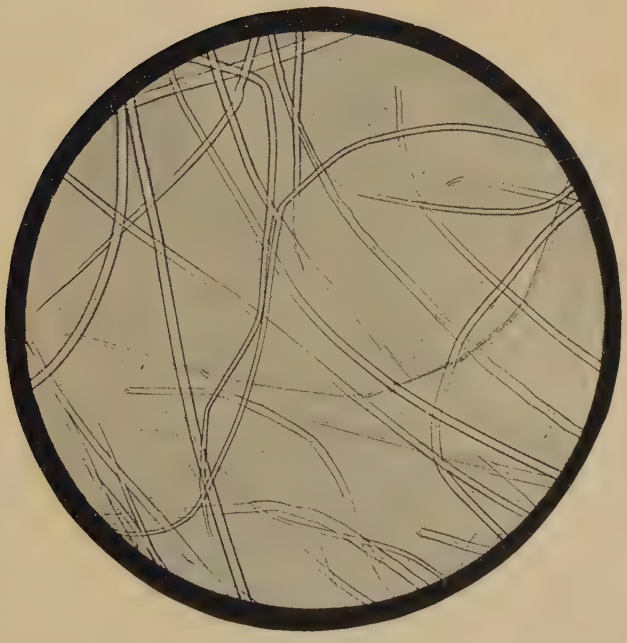


FIG. 2.

PLATE III.

FIG. 1.

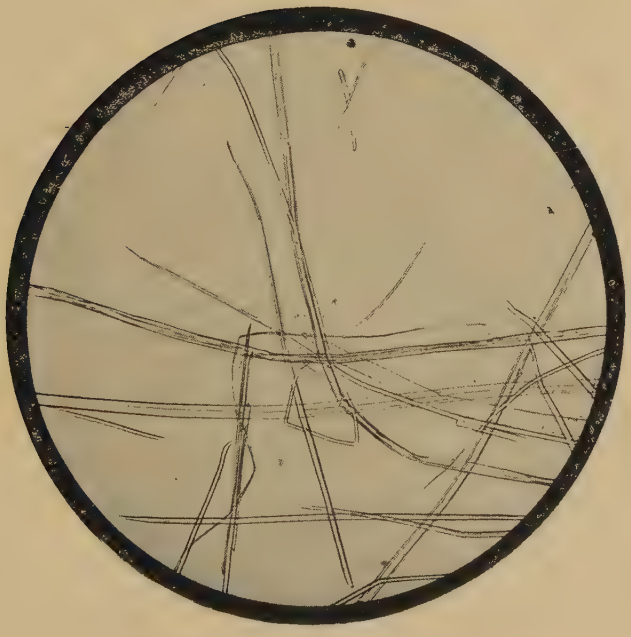


FIG. 2.

PLATE IV.

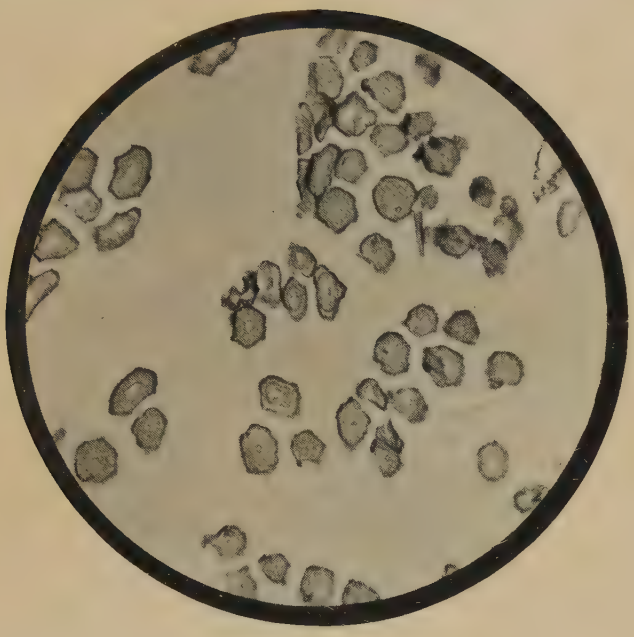


FIG. 1.

FIG. 2.

PLATE V.

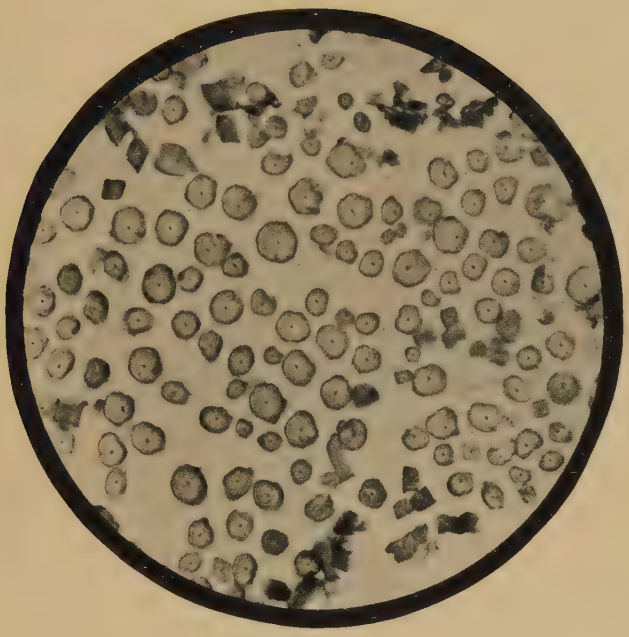


FIG 1.

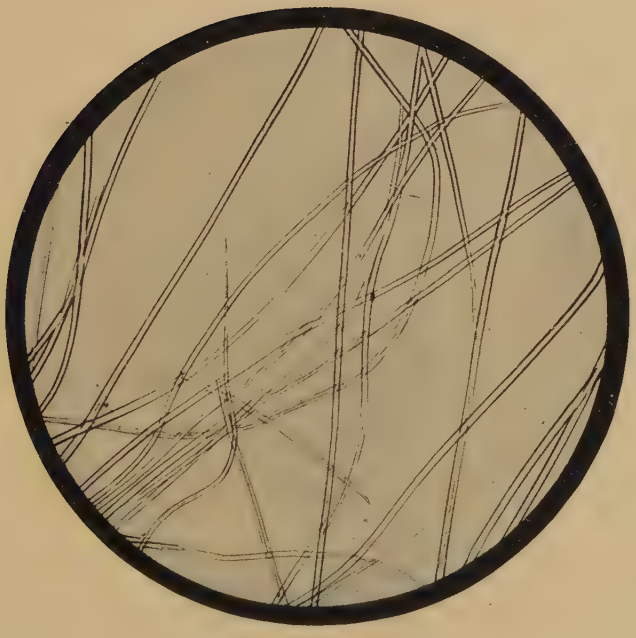


FIG. 2.

PLATE VI.

ABACÁ WASTE PAPER

RICHMOND: PHILIPPINE FIBERS, ETC.] [PHIL. JOURN. SCI., VOL. I, NO. 5.

COGON GRASS PAPER

COMBATING PLAGUE IN JAPAN.[1]

By SHIBASABURO KITASATO.

(From the Institute for Infectious Diseases, Tokyo, Japan.)

PLAGUE EPIDEMICS AND THEIR DETRIMENTAL EFFECTS.

In 1896 the epidemic of plague which had previously raged in India and Hongkong invaded Formosa, which from that time became a source of the dangerous pestilence. In this insular possession of Japan, a condition was produced in which the eradication of the etiological factor became almost impossible, and the situation began to menace the mother country. However, strict enforcement of preventive measures and quarantine precluded the entrance of plague from this into the main islands of Japan, but danger to our country was present from other sources, for the first case of plague encountered during this epidemic was found aboard a vessel which entered the port of Yokohama in 1896. The ship brought the dangerous germ from India and from southern China, with which regions Japan has frequent commercial intercourse. Since this event, steamers arriving at the same port and at Nagasaki and Kobe have brought in several cases of bubonic plague, but, as the discovery has always been made in time and preventive measures and quarantine have been promptly applied, infection has been avoided for the time being.

However, the origin of the epidemics in Japan has been located not in the patient but in inanimate objects. Incoming vessels from the infected regions—that is, from Bombay and Hongkong—began to introduce into the country the plague germ mingled with their freight, which principally consisted of cotton. The Government being unaware of this dangerous importation, the freight was allowed to land and as a consequence the infection rapidly spread in the principal trading ports. At first the epidemic prevailed among rats; afterwards it attacked human beings, with the result that many human lives were sacrificed, tens of thousands of yen of State money were expended, and the foreign trade of the country also suffered considerably.

The principal epidemics in Japan have been as follows: The first outbreak was that during the years 1899 and 1900. It began in Kobe;

[1] Read at the third annual meeting of the Philippine Islands Medical Association, March 3, 1906.

spread to Osaka, where its ravages reached a high mark, and then invaded Hamamatsu and Wakayama. The total cases in this epidemic numbered 230.

The second invasion was in 1902 and 1903, the source of this epidemic probably being in cotton which was imported from Hongkong. The initial cases occurred in Yokohama and it then spread to a district in Tokyo. The epidemic was stopped by the combined efforts of the two cities after it had claimed 71 victims.

The third outbreak occurred in 1905 and is still prevailing. Throughout different localities—namely, in Tokyo, Chiba, Kobe, Osaka, Kagawa, and Moji—a number of victims have succumbed to it. The disease appeared in Tokyo in the early spring, chiefly in the Fukagawa district, and it then spread to the Chiba perfecture, where a summer epidemic prevailed to a slight degree. The origin of the outbreak in Kagawa, lasting from May to the middle of June, appears to have been similar to that of the Osaka and Kobe epidemic and it was evidently due to direct contagion; its severity has been unparalleled in recent years. Two plague patients were found in the city of Kobe in August and the number of cases increased rapidly within the next few months, so that during the year the total number of victims amounted to 90. Next to Kobe, Osaka suffered most severely, there having been many cases since October of the past year, the number reaching 134 in three months. In both cities the outbreak spread throughout all the districts and it is still raging. Plague has also appeared in Shimonoseki and has claimed nine victims in that city. This epidemic has had no precedent both in its severity and in the number of its victims, the total of the cases during the year having reached 297.

The following table shows the regions of Japan in which the series of outbreaks occurred and the number of patients in each:

	Year.	Patients.	Deaths.	Principal regions of the epidemic.
First outbreak	1899	62	45	Kobe and Osaka.
	1900	168	153	Kobe, Osaka, Hamamatsu, Wakayama, and Nagasaki.
	1901	2	2	Wakayama.
Second outbreak	1902	14	9	Yokohama and Tokyo.
	1903	57	49	Do.
Third outbreak	1904	1	1	Kobe.
	1905	297	257	Tokyo, Kobe, Osaka, Chiba, Kagawa, Moji, and Nara.
Total		601	513	

The number of patients during the past year, distributed in different localities, is as follows:

Tokyo, 15; Chiba, 11; Osaka, 134; Nara, 2; Kagawa, 36; Kobe, 90; Moji, 9; total, 297.

In Japan the cost of preventive measures and quarantine has reached an enormous figure. During the first outbreak the city of Osaka expended more than 352,500 yen; during the second, Tokyo city spent 320,000 yen, although the number of patients there only numbered 15—i. e., 21,333 yen for every victim. These figures show the expense of plague outbreaks even when they are considered apart from their dreadful effect upon human lives. From the facts already given it will not be difficult to infer how much the present epidemic, which is raging in Kobe and Osaka with unparalleled vigor, will burden the financial resources of the country. Already the city of Kobe has given out 310,000 yen and Osaka city 470,000 yen for its prevention; and it is apparent from the present conditions that we will have to spend considerably more money to keep the plague at bay.

Such is the direct burden of plague upon the finances of a country, but this is not all; for the indirect detrimental effects must also be considered. This loss, indeed, can not be estimated, because it is a wide and far-reaching one, affecting both domestic and foreign affairs and one which can not be compared with that of an epidemic of any other kind which involves only its direct damage upon a limited community. Plague, indeed, is a fearful enemy to mankind.

Two methods of invasion are apparent from the studies of the epidemics in Japan: One is contagion from imported plague patients and the other by contact with the disease germ mingled with the freight brought in from some infected region. The nature of the preventive measures to be employed depends upon the source of the epidemic. If the invasion be by means of a plague patient, discovery is made easier and prevention or quarantine, as the case may be, can promptly be applied, so that the depredations of the disease may be confined within a small radius. On the other hand, if the organism is being propagated through the medium of rats, preventive measures are difficult; for, by the time infected rats are discovered, human beings have already become victims. Moreover, as a rule, by the time man receives the contagion from rats, the ravages of an epidemic have already reached serious proportions among these animals, so that the outbreak soon assumes a character which renders control difficult; the infection therefore spreads far and wide, affecting both men and animals. Such a result is illustrated by the first outbreak and by the present one in which Nagasaki and Kobe are the chief sufferers. The results at Chiba and Kagawa can be taken as an example of a case where the source of the epidemic was in human patients. In this outbreak we were able to keep the epidemic confined within a small locality by promptly applying the usual preventive measures—that is to say, before the rat was attacked by the germ. We can thus see that the same preventive measures may give different results in different cases.

In every epidemic it is difficult to ascertain the exact circumstances

under which the plague invasion occurs. This is especially true when the medium of propagation is outside the human patient, and it is notably the case where rats are the agents. So far, in every case, the plague outbreaks in Japan were first evidenced in localities which have direct communication with foreign countries and from these points the spread to the regions of the interior occurred. Moreover, the first case in any place which subsequently became a source of plague was invariably associated with freight imported from India or from Hongkong. The first epidemic owes its origin to a steamer which entered the port of Kobe with a cargo of raw cotton and Chinese rice from Bombay and Hongkong. The second one may be traced to a vessel which came to the port of Yokohama with freight consisting of raw cotton. The present great epidemic which prevails in Osaka and Kobe is due to a steamer which anchored in Kobe Harbor laden with a consignment of raw cotton from Bombay. These statements demonstrate the almost identical origin of the fatal pestilence in each instance.

As a rule, the plague germ on entering these trading ports does not immediately attack man; it first infects rats and by the time the first human victims are discovered, the epidemic has assumed a well-advanced form; this fact has been demonstrated on several occasions. The present epidemic in Osaka may be considered as an example. In February it was preceded by the discovery of infected rats, but only during May of the same year did human victims begin to appear, thus showing how deep rooted was the source of the infection.

The season during which an epidemic occurs has a marked influence. Thus it is apparent that a winter outbreak is generally of a most chronic character; it rages for a long period with great severity, spreading over a large extent of territory. The first invasion, the present epidemic in Osaka and Kobe, and the second one in Tokyo and Yokohama, belong to this class. A summer epidemic is usually acute in character and as a rule is spread by contagion. It may be severe though of short duration, and it is limited to a small area. The epidemics in Chiba and Kagawa during the past year and that of Hamamatsu in 1900 were of this nature. It should be noticed that during a winter epidemic a large number of infected rats are met with, while in a summer one but a small number or even no infected rodents are encountered. (See Pl. I.)

PREVENTIVE MEASURES.

As the plague epidemics in Japan, according to observation, originated in the Indian Peninsula, in Southern China, and in Formosa, the first and most urgent step to prevent the introduction of the disease was to establish quarantine against vessels coming from these regions. With this end in view, quarantine stations were erected at Yokohama, Kobe, Nagasaki, Moji and other principal trading ports and the necessary measures enforced as strictly as possible. So far, several cases of plague

have been discovered on board vessels coming from the infected regions; but as a result of the strict quarantine, the danger of contagion has been prevented. When a ship is found to have plague infection on board, all communication with the land is stopped, measures are taken to destroy the rats, and other sanitary precautions are employed. In order to provide the means for killing rats on board ship, auxiliary vessels especially fitted for that purpose and similar to those used in Hamburg, Germany, are recommended. We now have several of these at Yokohama, Kobe, and Moji, and they will be employed during the present year.

The Department of the Interior of the Japanese Government, through the Bureau of Public Health which belongs to that Department, names officials who are to meet to discuss and execute measures for the prevention of infectious diseases. These committees consist of physicians and surgeons with assistants and quarantine commissioners. Each municipality or prefecture has also its established board of health, which consists of one physician, several assistants, and a number of inspectors. This organization is placed directly under the control of the police department, and it takes charge of all matters relating to infectious diseases. The principal prefectures and districts are provided with isolating hospitals to receive patients and with laboratories for investigation and these boards of health carry out the necessary preventive measures. In case of a plague outbreak, the prefectural government increases the number of health officials so as to meet the emergency. When an epidemic of an unusual nature takes place, an imperial receipt is issued by means of which the organization of a special board consisting of commissioners, inspectors, clerks, and watchmen is ordered for fighting plague. In addition, several councilors are appointed to submit advice relating to the matter. The municipal government of Osaka has increased its staff by 311 officials and a number of councilors because of the present outbreak.

In Japan all affairs relating to health and sanitation, particularly to the prevention of infectious diseases, are referred to local administration, the execution of the necessary measures being carried out by the aid of the police. The expenses required for the purpose are shared by the people of the locality in which the disease occurs, aid also being given from the financial resources of the prefectural or municipal government. In case of an outbreak of contagious disease, the Central Government will give assistance to the local ones to an amount not exceeding one-sixth of the total outlay. However, in the case of plague, the Central Government has spent and is spending an amount enormously in excess of that fixed by regulation.

The Institute for Infectious Diseases acts as councilor to the Government in matters relating to health, and it especially advises in regard to the preventive and sanitary measures which are to be taken against

infectious diseases. When a plague epidemic exists, our Institute, through governmental appointment, furnishes those commissioners and officials who are to take charge of the preventive and sanitary measures. It has a plague laboratory constructed in conformity with the most advanced methods and in this place pest serum and vaccine are prepared for the use of the entire country. As a part of its work the institute gathers a number of physicians and surgeons throughout Japan in order to give them instruction in bacteriology and epidemiology. The number who have finished this course at present amounts to 1,293, and these physicians are scattered throughout the country. At least a portion of them are now actually engaged in important work in hygiene and preventive medicine. As these specially educated physicians and surgeons are distributed throughout Japan, it is a matter of ease in an emergency at once to gather several hundreds of commissioners. To fight plague successfully requires a large number of trained men, and the country owes its thanks to the Institute for rendering so many available.

Such, in brief, is the account of the organization of the preventive work which so far has been instituted in Japan. However, I must here express my sincere admiration and surprise at the manner in which your country is protected from pestilence. You have medical officials stationed at the principal ports of the world which plague frequently haunts, so that inspections are made at the places from which vessels clear. I believe preventive measures against plague to be the most urgent need of the age, but in order to be of permanent good they must include, as is the case with the United States, not only temporary means for preventing the intrusion of the disease to be enforced at the ports of entry, but also medical officials to be stationed in infected regions, at which points any vessels starting for the country in question can be strictly examined. I am of the opinion that it would be advisable to place such officials at Indian and South China ports to which the plague outbreaks in Japan have been traced.

In combating plague, the quarantine of ports, however strict and complete it may be, can not safely be relied upon and for this reason general provision throughout the country must be perfected against infectious diseases. As plague can not be classified with the ordinary ones of this class, the regulations to meet such emergencies in Japan were found in general to be unsuitable, so that the Government was compelled to remodel them in order to meet the condition. The principal features of the new regulations are as follows:

1. Authority for disinfection, isolation, and quarantine is given. Measures looking to the prevention of the disease are to be enforced not only against the living patients and in respect to the houses and furniture occupied and used by those actually stricken with plague, as well as of those who are only suspected of having the infection, but also in regard to the bodies of those dead with plague.

2. To prevent the spread of the infection, as many rats as possible are to be killed.

3. The period of isolation of suspected patients is not to be less than ten days.

These modified regulations were based upon the experience of several years. In carrying out measures of disinfection it is necessary to extend the area to be covered as far as possible, as the plague germ is very easily propagated. It is also true that bubonic plague often develops into that of the pulmonary or pneumonic type and in that event the disease not infrequently infects by direct contagion therefore, especially in times of epidemic, quarantine and isolation must be strictly enforced. It was thought necessary to fix the time of isolation at ten days because of the fact that the incubation period of the disease lasts from six to seven days. The killing of all rats which it is possible to secure was deemed a necessity, as these animals have the closest connection with plague. The above principles were applied where the intrusion of the pestilence was suspected even before the formulation of the new regulations.

In attempting to catch rats it is important to remember that traps and appliances should be set in all buildings, and it is imperative in those which contain cotton and grain, in which the plague germ is most liable to be retained. I gave warning in this respect a few years ago and as a result the municipal government of Tokyo has passed an ordinance respecting buildings and warehouses which provides that all buildings must be constructed in a manner to prevent their becoming an abiding place for rats. A similar regulation has been adopted in other cities and prefectures, especially in those having direct connection with foreign countries. These legal acts appear to be rather despotic, but nevertheless they must be deemed necessary in view of the dreadful character of the disease which is propagated by these rodents. I believe that the extension of similar regulations to dwellings so as to render all of them rat proof would in the future generally lessen the danger from the infection. Such a step has yet to be taken.

SANITARY WORK.

The principal undertakings established for the enforcement of preventive measures are (1) bacteriological examinations; (2) search for patients; (3) killing of rats, disinfection, and the application of sanitary methods; and (4) disposal of patients and of infected articles. The work may briefly be described as follows:

The bacteriological laboratories in the different districts and prefectures are for the study and diagnosis of plague, and in times of epidemic they are used solely for this especial purpose. In such cities as Kobe, Osaka, Yokohama, and Tokyo, which are most frequently threatened by pest, the Government for several years past has been encouraging

the destruction of rats by buying all which are killed or captured by the people. This practice has a twofold purpose—one the prevention of an epidemic, and the other the ascertaining whether any infected animals, the presence of which usually precedes an epidemic among men, are existent. An immense number of rats is bought by the Government and each one of them is examined bacteriologically. (Pls. Nos. XIV–XVI picture their examination in the laboratory of the Tokyo Metropolitan Police Board.) In this latter place from 3,000 to 4,,000 rodents are examined daily even in ordinary times, but when an epidemic occurs the number is increased to an enormous figure. As plague outbreaks in Japan are usually preceded by rat infection, these examinations are to be regarded somewhat in the light of a reconnoissance. The utility of this precaution is illustrated by the fact that in 1904 an infected rat was discovered in Yokohama before any human victim had been found and as a result the source of the infection was sought and finally traced to a British steamer, the warning being given in time. During epidemics, the examination of rats is even more necessary, for it is only by such a process that the condition and the manner of propagation of the pestilence are actually known.

To judge from the experience of the past, it can be suggested that in examining rats particular attention should be paid to their submaxillary and cervical glands and to the spleen. These organs in most cases show the evidence of infection, if there be any. The inference to be drawn is that the rat receives the plague germ through the mucous membrane of the mouth and throat.

An important work during an epidemic is the bacteriological examination of specimens obtained from the patients and the dead, for the diagnosis must depend upon both clinical and bacteriological observation. In suspicious cases, material for investigation is taken from the affected parts, such as the glands or skin. The sputum of the patient is also frequently subjected to examination. In the dead, the heart's blood and spleen and the contents of the glands or lungs are scrutinized. Microscopical examinations are undertaken, cultures are made and animal experiments are performed with the specimens which are gathered. Agglutination by a pest serum, of the bacteria obtained is also studied. Obviously it is often difficult to assure one's self of the discovery of an infection by any of these means, but there are many cases on record where suspicious substances such as cotton, filth, and rotting grain harbored the *Bacillus pestis;* as an illustration I will cite the fact that in 1899, in Osaka, cotton waste was found to contain the plague organism.

The searching for patients, especially when the first invasion of plague is suspected, is also an important portion of the preventive work. Physicians are expected by law to report any infectious disease which they discover, but such reports are in most cases not reliable; indeed, during

an epidemic period this source of information reveals only about one-tenth of the whole number of cases actually existing. In the localities which have never before been visited by plague, the physicians themselves are ignorant of the nature of the disease and they may thus permit an outbreak to spread rapidly. This unfortunate condition was illustrated in Kagawa during the past year.

As a means of promptly seeking out patients in places which are frequently in danger of an outbreak of pest, the physicians attached to the police are given authority to examine the bodies of all persons dead from acute, febrile diseases. During epidemic periods such examinations give results parallel to those obtained by the investigation of the rats which are caught, and that such precautions can not be neglected is shown by the experience obtained in the past. The following table gives the number of plague patients discovered during the outbreak in Osaka and Kobe during the past year:

	Osaka.	Kobe.
Physicians' reports	49	30
Inspection of dead	27	26
Inspection of houses	34	33
Among the isolated suspects	20	0
Miscellaneous	4	1
	134	90

The value of the inspection of the dead is apparent, for the foregoing table renders it evident that in Osaka 27 and in Kobe 26 instances would have occurred in which bodies which really were infected with plague would have been regarded as being dead of other diseases and thus the number of foci of the epidemic would have been increased.

The inspection of apparently healthy persons living in an infected locality or its vicinity is not an easy task, though a very necessary one. Epidemics are most liable to prevail in places where ignorant people reside and this fact alone greatly hinders the work of the health inspectors. Only by reason of their devotion to duty and work can their efforts be successful. The value of their work was illustrated during the outbreak of the second epidemic in Tokyo. In the latter city, with the exception of three early cases out of a total of 13, a suggestion and warning was given by the diagnosis of plague in persons apparently healthy and these persons were removed and isolated. During the present epidemic in Osaka not a few of the dangerous patients were discovered by the general inspection of healthy persons. However, the task of finding plague cases by such a method becomes more difficult in proportion as the epidemic spreads and the patients are found scattered over a wider area. As aforesaid, plague in a patient must frequently be diagnosed by both a clinical and a bacteriological examination and the application of such tests must be undertaken as speedily as circumstances will permit. The absolute diagnosis is usually effected within

forty-eight hours after the finding of the suspicious patient or of the dead body and during the examination the patient or the dead body is to be regarded as if it were a genuine instance of plague infection.

Even during ordinary times, the killing of rats is enforced in localities where imported freight is stored or where laborers live and this enforcement is made general when there is danger of an outbreak of plague. At least two days before the general sanitary precautions outlined above are applied, rat catching and killing devices, such as traps and poisons are distributed to every dwelling and warehouse. Formalin vapor or sulphur dioxide is used in buildings which can be tightly closed. All localities which are constructed so as to permit of the abode of rats are rebuilt, the sewage is improved, and all filth is burned. The above constitute the measures employed for removing and killing rats. The occupants of the dwellings in which infected rats are frequently found, or in which plague patients are discovered, are removed and the whole house disinfected and rendered unfit for rodents by the sanitary measures adopted in the killing of rats; in order more effectually to destroy the latter, galvanized-iron walls are erected around such houses and all exits of the sewers are closed by means of metal nets. If the infected area is extensive it is divided into small sections, and the same method is applied to each one of these. The first steps in sanitation after these precautions have been taken are to search for and destroy the rats, to disinfect the furniture and finally the entire building. For the latter purpose carbolic acid, corrosive sublimate and lime are used, articles of an especially suspicious nature being at times steamed, boiled, or burned; all of the disinfected objects are ultimately exposed to the sunlight. In case the building is situated in such a manner as to render the application of sanitary measures difficult, it is sometimes desirable to disinfect by burning the entire edifice. Such extreme measures I believe to be especially justifiable where the infection has not as yet spread to a large area, and they are not infrequently made use of in Japan. The galvanized-iron fence or wall which is erected before fire is set to the premises prevents the rats from finding their way to the neighboring houses, and thus possibly spreading the disease.

However, the difficulties attendant upon the entire destruction of houses for purposes of disinfection are in some instances insurmountable, and this is particularly the case when plague patients and infected rats are scattered over a large area. The present epidemic in Osaka and Kobe illustrates such a situation. If extreme measures were to be applied to these cities practically whole districts would have to be burned.

As has been remarked above, the zinc fences prevent the escape of rats during the work of disinfection and their effectiveness in segregating an entire area before an epidemic becomes general has been abundantly illustrated during the outbreaks in Yokohama, Kobe, and Tokyo. These walls present a most peculiar appearance. (See Pls. X–XII.) Their

height varies according to the circumstances, but usually it is about 3 feet with a foot or two buried in the ground. Rats can neither climb such a wall nor burrow under it. The use of zinc for such a purpose is apparent, for it is not liable to rust as are other metals, and it may be used repeatedly. These walls have been utilized during every epidemic, the largest one being constructed in Tokyo in 1903. In this instance the area inclosed was three-fourths of a mile square, with partitions dividing it into several sections. In addition, every other place where infected rats were found was inclosed within other fences and the total length of the walls so used measured 29,148 feet, or about 4 miles.

The discovery of a case suspected of having plague is promptly followed by the proper measures to prevent further spreading of the disease. Inspecting physicians hurry to the patient's residence and, if he really proves to be attacked by the pest, the victim is at once conveyed either to a hospital for infectious diseases or to one of isolation where proper treatment can be given. Should a dead body be discovered infected with the plague bacillus, the cadaver is first disinfected externally and then cremated. Each member of the family and the contacts in the neighborhood are then sent to an isolated detention dormitory where they are given a daily examination during their term of quarantine. They are subjected to all possible means of disinfection and prophylaxis, including the conferring upon them of passive immunity by inoculation with pest serum, whereas those from the neighborhood who are in less danger of having contracted the disease are given pest vaccine. In every epidemic this serum and vaccine have been generally used, over 10,000 individuals having been inoculated, but we have been unable to obtain exact statistics as to the value of these remedies during the epidemics on the main Japanese islands.

However, during the outbreak in Tainan, Formosa, occurring in 1901, the conditions were such that we were able to obtain valuable statistics and the large number of persons which were inoculated with pest vaccine gave suggestions as to the value of vaccination. Of 10,876 persons inoculated in Tainan only seven were attacked by plague; while out of about 40,000 persons who failed to receive this treatment, more than 500 were infected. From such statistics it is not difficult to believe in the favorable results of vaccination, although we are not yet in a position definitely to determine its value.

Those plague commissioners and officials who from the nature of their duty frequently came in contact with the patients, have received prophylactic inoculations of the serum (16–20 cubic centimeters). Not one of these individuals has as yet been infected. Instances are many in which the value of the serum as a preventive has apparently been demonstrated.

For the treatment of plague patients two methods may be recommended—one the extirpation of the buboes and the other the inoculation

with serum. The efficiency of the extirpation and of the serum treatment depend on the stage of plague development which exists at the time they are instituted; when performed in an early stage, a favorable result may be expected, but in a later one these measures become futile. As a consequence, it is important to obtain a positive diagnosis as early as possible.

That good results may be obtained from serum treatment in such cases admits of no dispute. During the first outbreak in Osaka, Yersin's serum was used, but owing to the scarcity of the supply of this remedy, the results fell short of our expectations. Since 1900 our institute has been preparing the serum to meet with the constant demand. For the patients actually suffering from the disease, comparatively large quantities (200–240 cubic centimeters) are required for inoculation, and although we are not in a position to ascribe to the pest serum a value as absolute as to the diphtheria serum, there is no doubt of the efficacy of the former remedy. The following facts demonstrate this:

A series of experiments was conducted in the Tainan isolation hospital (Formosa) with the view of comparing the results of the serum with those of an early extirpation of the buboes and general systematic treatment. Of the 56 patients treated by the latter method, 35 (62.5 per cent) died of plague, while out of the same number inoculated with serum the death rate was only 33.9 per cent. From these experiments it is seen that the use of the serum reduced the death rate by about one-half. Our experience during the epidemics in Japan has shown that the most effective treatment is that in which both serum inoculation and extirpation of the buboes are performed in as early a stage of the disease as possible.

RATS AS THE PROPAGATORS OF PLAGUE.

The fact that rodents are always closely connected with an outbreak of plague (in all times and places) admits of no dispute. The epidemics in Japan have invariably been traced to rats.

Obviously these animals have a high susceptibility to the pest infection; their habits also constantly bring them in contact with filth in which the plague germ is present, besides which they feed upon one another. These facts must favor the spread of plague. The finding of human victims of the pestilence is almost invariably preceded by the discovery of plague-infected rats. Hence the killing of rats must be resorted to as the first and most important step in the prevention of an epidemic. In the first outbreak in Osaka and Kobe the pestilence was gradually stopped by an urgent effort directed at destroying these rodents; and the ones in Tokyo and Yokohama were confined to a small area by the strict enforcement of these same measures. The number of rats killed in Tokyo since 1900 and up to the present time amounts to the enormous figure of 4,820,000—that is to say, the average is more than 800,000 a year. In other words, if these dead rats were laid side by side they would extend for a distance of

over 75 miles. The price paid by the local government for these animals, which were bought from the people, in Tokyo alone has amounted to 160,000 yen.

However, the extermination of rats is complicated by the fact that the rodent increases at an enormous rate; as a rule within one month of pregnancy the female gives birth to five young ones at a litter, and the young reach puberty and become pregnant at the age of three months; thus these animals multiply in a geometric progression. Furthermore, if rats are destroyed by artificial means, such destruction only lessens the struggle for existence and then the rate of multiplication is much increased. In Tokyo more than 4,800,000 rats have been killed; yet we can hardly notice any considerable decrease in the number of these animals.

In Japan, for killing rats, poisons such as arsenic and phosphorus, together with traps, are chiefly used. The typhoid bacillus of the rat, which has been effectively used for killing field mice, has been found useless for house rats and therefore we no longer employ it.

Someone has offered the following suggestion for the disposal of the usual breed of household rats (*Mus rattus*), which unfortunately is the species most liable to be attacked by plague. This suggestion is to introduce *M. decumanus,* which is a persistent enemy of *M. rattus,* and which is comparatively more resistant to the infection. Such a suggestion appears to me impracticable for from my actual observation it is evident that so far as the epidemics in Japan are concerned, the *kind* of rat has been of very little importance in propagating plague. Moreover, the results of biological researches tend to confirm the fact that although two distinct species of rats are found, the one most prevalent in Japan is a race which is a mixture of the two and which is also susceptible to plague. Such a fact rather contradicts the assumption that the two species are natural enemies to each other. Therefore, the above recommendation can hardly be taken as a basis for preventive measures against plague.

The best way to destroy rats in connection with the restriction of pest is to prevent their abiding in or at least to expel them from human habitations. In order to accomplish this purpose I suggest that all buildings be rebuilt according to a plan which will serve this end. This particularly applies to Japanese houses, because in most cases the latter are built of wood, and such buildings are liable to provide quarters for rats. I understand that the United States is planning a reconstruction of "Chinatown" in San Francisco. I highly approve of such a step in view of the situation of that port, which is constantly threatened with a plague invasion. In Manila, also, the cause of the recent fortunate decline of the plague epidemic, I believe, can chiefly be attributed to the rebuilding of the city since the Islands became a possession of the United States.

In Japan, the insular territory of Formosa which has been invaded by plague is now being surveyed by the sanitary officials, and the buildings in the central part of Tainan City have already been reconstructed so as to keep the rodents out. As a consequence, the ravages of the pestilence are now practically confined to the villages or to groups of unsanitary habitations of the natives, who live with the rats and permit these animals to flourish.

The following table demonstrates that during a plague epidemic the number of infected rats runs parallel with that of the patients discovered:

	Osaka.		Kobe.	
	Patients.	Infected rats.	Patients.	Infected rats.
May	1	1	0	2
June	0	0	0	0
July	0	0	0	0
August	0	0	2	3
September	0	5	8	11
October	6	39	4	17
November	45	119	36	151
December	82	634	40	405

The number of rats examined during the past year in Osaka amounted to 1,195,116. Of these, 19 infected animals were found previous to May, making a total of 817 in all. In Kobe 553,616 rats were examined; the number of infected ones can be ascertained from the table. From this it may be inferred that the prevalence of the human infection bears a direct proportion to the number of infected rats found, and that the extent of the epidemic may be known approximately by the area of the localities in which infected rats are encountered.

Our attention is particularly directed to the fact that the fiercest ravages in every epidemic are evidenced in winter rather than in summer. This may be due to the resistance which the pest bacillus has to cold, although it appears that this point needs further consideration. A particularly interesting fact is that in both Osaka and Kobe the number of infected rodents found during the last two months of 1905 was very large as compared with the number of plague patients, and also the statistics up to the middle of January of this year show a remarkable feature in that there were 240 infected rats against three patients in Kobe, and 179 against nine patients in Osaka.

During the present epidemic I have had opportunity to make close observations as to the prevailing conditions, and have discovered an interesting fact concerning the habits of the rodent. Rats generally live on the ceiling below the roof, but in winter they change their abode by removing to the ground just below the floor. Therefore, in order to discover the openings which harbor the rodents, the ground should be dug to a depth of 1 or 2 feet, the rat-holes are thus exposed and the animals can be exterminated. This method, owing to the subterranean habit of rats in winter, invariably secures a great number. These animals are

gregarious and consequently, if one of their number becomes infected in the winter quarters, then many must inevitably fall victims to the disease, but obviously there is less danger from rodents which live underground and apart from human habitations than there is from those dwelling in the houses themselves. It is for this reason that during winter epidemics a very large number of infected rats, as compared with human patients, is encountered.

The weak rodents are constantly menaced and frightened by the strong ones, so that the individuals which have been attaked by plague must maintain constant vigilance so as to be able to flee from their pursuers. As a weak rat has not sufficient strength to climb a fence or to reach any considerable height it is obliged to wander on the surface of the ground, thus providing for the spread of plague.

The large number of children who are infected by playing on the ground would seem to emphasize the fact that in this situation the bacillus is most readily encountered. The following table shows the number of children infected with plague during the winter epidemics:

Number of patients.	1900, Osaka.	1905.	
		Kobe.	Osaka.
Total patients	144	90	134
Patients under 15 years	56	36	51
Percentage	38.8	40.0	38.06

From the above it will be seen that the number of patients under 15 years of age is more than one-third of the total. (See also Pl. II.) The subterranean and gregarious habits of rats, the sowing of the plague germ on the ground, and the large numbers of young patients—all of these are closely connected with winter epidemics.

It is apparent that measures for killing rats must of necessity involve the application of biological knowledge bearing on the habits of these animals, but our knowledge in this respect has yet to be perfected. The methods of destruction used in Japan to-day consist in the use of poison or of traps. Such means have only a temporary effect and the results of their use can not be considered to be of sufficient permanence to root out the evil. The destruction of rabbits in Australia was undertaken in such a way as to produce a permanent effect and we have much to learn from the method involved. It was based on the fact that the rabbit is a polygamous animal and therefore if as many females as possible could be destroyed by artificial means, the end would be a struggle among the males for their possession. The result of such a practice, of course, can not be expected in a brief period, nevertheless it is of a permanent character. I suggest that something of this nature be planned for the destruction of the rodents.

CONCLUSION.

In conclusion I desire to suggest what I consider to be an ideal plan for combating plague. I believe that the fatal pestilence, however obstinate its ravages and terrible its effects, could be fought and vanquished by the persistent efforts of man and I also believe that where human endeavor, backed by money, is determinedly directed against it, it must yield. But the efforts, however laborious, the money, however vast, can be of no value unless they be accompanied by the application of scientific knowledge. The danger of plague invasion through open ports must increase in proportion as international commerce progresses and maritime enterprise advances. Again, where man has fixed his abode the rodents accompany him to share it; and the unwelcome creature becomes the cause of the dreadful evil. In ports which vessels from infected regions frequent, an epidemic of the pestilence may not be difficult to exterminate. But if infection after infection is repeated from fresh importations the expenditure of large sums of money and much tedious effort become involved. In regions like India and southern China, plague appears to be deeply rooted, prevailing almost incessantly for several years and during each year attacking more than 200,000 victims. It is apparent that we can not avoid the danger of invasion by the pestilence at any moment, so long as we do not cease intercourse with these regions. To be content with the mere placing of quarantine on the incoming vessels from these places or of enforcing rat killing and other sanitary measures in the open ports seems to me to be but imperfect protection. Why not extend the combat to the source of danger and destroy the cause of the evil permanently? Plague is not only objectionable to the people of one locality but it is an enemy of mankind in general. All civilized nations must fight this common enemy. I believe there should be an international conference to discuss a plan to collect money and to organize an international army to combat and vanquish this disease wherever it appears. Expeditions should be sent to the interior regions of India and south China. The cost of such an enterprise would be only a small part of what the civilized nations are constantly expending in keeping armies and navies. Even the amount which every country is spending for the prevention of the pestilence would suffice. My suggestion only lacks a leader, and I see that the United States, one of the greatest nations of the earth, has such a leader in the person of its President, Theodore Roosevelt, who has already done so much for humanity and whose noble works are being admired by the whole world.

ILLUSTRATIONS.

PLATE I. Table showing the number of plague patients and infected rats during the year 1905 in Osaka and Kobe.

II. Diagram showing the ratio of mortality with regard to the ages of the patients.

III. Disinfecting dormitories of a cotton firm at Fukagawa, Tokyo.

IV. Disinfecting the interior of the compound of a cotton firm at Fukagawa, Tokyo.

V. Disinfecting, by exposing to sunlight, sacks of rice suspected of infection, Tokyo.

VI. Disinfection of infected houses at Fukagawa, Tokyo.

VII. Houses after disinfection, Tokyo.

VIII. The entrance to an isolating barrack for healthy people, Tokyo.

IX. General view of isolating barrack for healthy people, Tokyo.

X. Showing area in which disinfection of houses and the destruction of rats is being carried on. The infected area may be seen inclosed within a zinc wall.

XI. Warehouses located in an infected region and inclosed by a zinc wall.

XII. Rat-proof zinc wall inclosing the buildings of a cotton firm, Fukagawa, Tokyo.

XIII. Excavations made in searching for rats in the ground, under the first floor of the warehouse of a cotton firm, Tokyo.

XIV–XVI. Bacteriological Laboratory of the Tokyo Metropolitan Police Board. Examination of rats for pest infection.

XVII. Medical officers, inspectors, and policemen appointed for the purpose of combating plague in the year 1903.

XVIII. Male patient. Inguinal and femoral bubos (cured).

XIX. Female patient. Infection of the eyes with pest bacillus (fatal case). Primary lesion, right eye; secondary lesion, left eye.

XX. Pest bubo of the axillary and cervical glands (case recovered).

XXI. Infection of left submaxillary gland before the abscess was incised (case recovered).

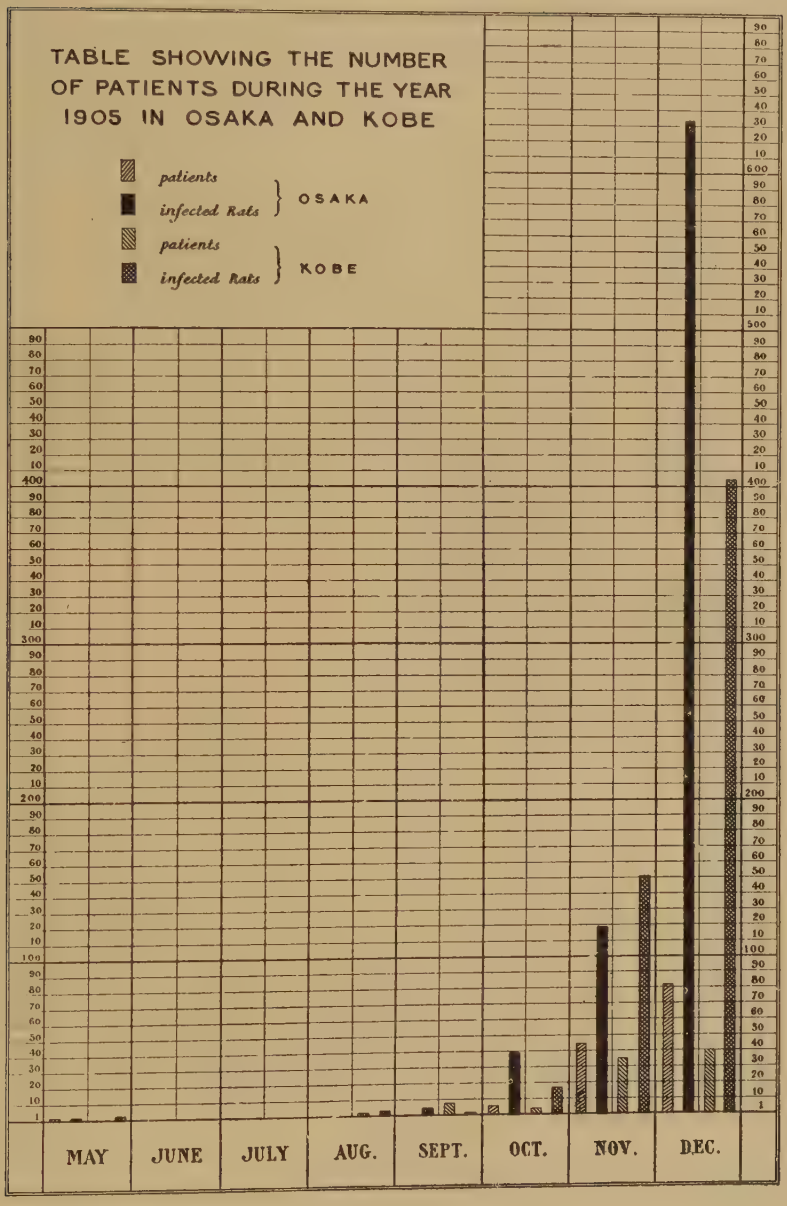


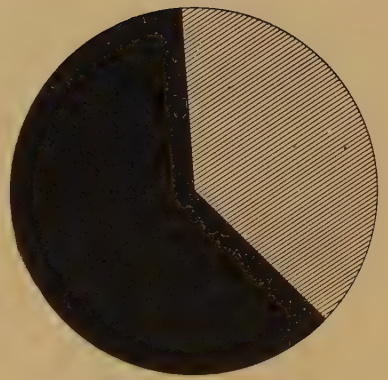
TABLE SHOWING THE NUMBER OF PATIENTS DURING THE YEAR 1905 IN OSAKA AND KOBE
patients
infected Rats
OSAKA
patients
infected Rats
KOBE
MAY
JUNE
JULY
AUG.
SEPT.
OCT.
NOV.
DEC.

PLATE I.

DIAGRAM SHOWING THE RATIO OF MORTALITY WITH REGARD TO THE AGES OF THE PATIENTS

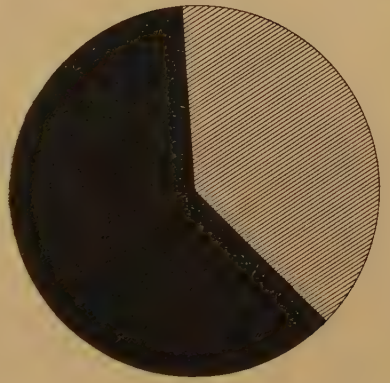
under 15 years.

above 15 years



1899 1900
OSAKA

1905 OSAKA



1905 KOBE

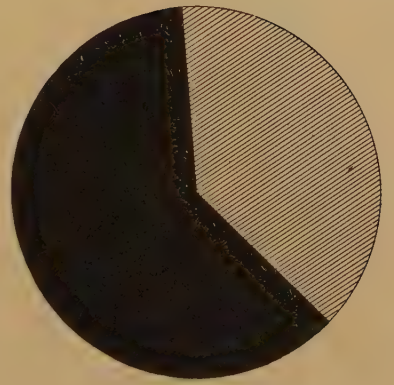


PLATE II.

PLATE III.

PLATE IV.

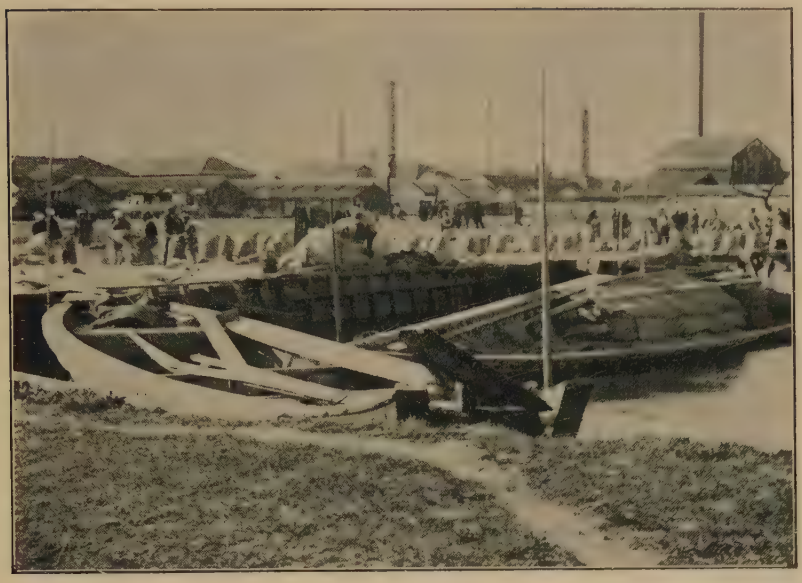


PLATE V.

PLATE VI.

PLATE VII.

PLATE VIII.

PLATE IX.

PLATE X.

PLATE XI.

PLATE XII.

PLATE XIII.

PLATE XIV.

PLATE XV.

PLATE XVI.

PLATE XVII.

PLATE XVIII.

PLATE XIX.

PLATE XX.

PLATE XXI.

OBSERVATIONS ON THE EPIDEMIOLOGY OF DYSENTERY IN JAPAN.[1]

By K. Shiga.

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Before discussing my own work on dysentery I consider it to be advisable to give a brief outline of the course of the epidemics of dysentery in Japan, for I believe that in no land other than our own has this disease taken such deep root or appeared with such destructive results. Dysentery for a long time has been prevalent in Japan, its beginning probably antedating the present time by hundreds of years, but reliable statistics are only available during the last three decades.

The Japanese Empire extends from 21° 48′ to 50° 56′ north latitude, and following the geographical configuration the country is divided into seven provinces which, as a rule, are used as the units in statistical work. Therefore the southern portion of Japan is tropical or subtropical, whereas the northern part belongs to the cold zone. Amœbic dysentery occurs in Formosa, but, up to the present time, epidemic or bacillary dysentery has not with certainty been proven to exist in that island; in the island group at the extreme north (*Chishina*) dysentery has not been observed at all. The mainland of Japan, on the other hand, is in the temperate zone, and it is exactly in this region that epidemic dysentery appears; and therefore, for the purposes of this paper, only the mainland needs to be considered. This consists of four islands—Kiushu, Shikoku, Honshu, and Hokkaido; Honshu is again divided into the western, central, and northern provinces. The following table gives the degrees of latitude occupied by the regions in question:

Kiushu: From about 31° to 33° 58′ north latitude.
Shikoku: From about 32° 42′ to 34° 34′ north latitude.
Honshu: Western province from about 33° 30′ to 35° 40′ north latitude.
Central province from about 34° to 37° north latitude.
Northern province from about 37° to 41° 38′ north latitude.
Hokkaido: From about 41° 21′ to 45° 30′ north latitude.

If we study the course of the epidemics of dysentery in these six divisions of Japan we encounter a very interesting picture. In the past

[1] Read before the third annual meeting of the Philippine Islands Medical Association at Manila, March 3, 1906. Translated from the German by P. C. F.

thirty years two extensive outbreaks have traversed Japan from the south to the north, the first, and lesser one, beginning in Kiushu in the interval between 1883 and 1885. It was only in 1885 that it extended into Shikoku and in the next year (1886) into the western parts of Honshu, from which latter portion of the country it soon disappeared, not reaching farther toward the north. The second and larger one, in its movement, can be described very graphically. Between 1892 and 1894 a great epidemic of the disease again appeared in Kiushu, the number of the sick reaching nearly 45,000 to 50,000; in 1895 it suddenly lessened so that the patients decreased to about 14,000, and in the next year they further diminished to about 6,000. Meanwhile, in 1893 the epidemic pushed forward into Shikoku, reaching its maximum in 1894, the number affected being 34,600, and from this point it extended into Honshu, however, only being observed in the western provinces of this district in 1895—that is, two years after its appearance in Shikoku. In 1896 the disease extended to the central province, and during three years it ravaged that district with frightful intensity. Just as it was beginning to diminish samewhat in this latter region it suddenly appeared in the western provinces, in which portion of Japan it reached its highest point, so that there the number of cases reached 60,700 in 1899. Up to the present time this great epidemic has never appeared with any degree of intensity in Hokkaido, the northernmost of the large islands of the Empire, probably because of the cold climate—for in that portion of the country we have only encountered some hundreds of cases in one year.

As has been seen, the great waves of the epidemic of dysentery gradually rolled from the south toward the north, the greatest amplitude in one and the same region remaining during one to three years. After reaching its maximum, it suddenly diminished, to repeat itself, as statistics show, at intervals of from ten to twenty years. This interesting phenomenon can probably be explained through the immunity to dysentery which persists for a certain time after infection with the disease. About thirty years ago (1879) an extensive epidemic of dysentery appeared in the northern provinces of Honshu although, at about this time, only a few cases were observed in other portions of Japan. I regard this outbreak in the north as the termination of a great one which probably also traveled from the south to the north and which represented the ultimate extensions of the epidemic. Owing to these considerations I believe the conclusion to be justified that great epidemics of dysentery will threaten us every ten to twenty years if we can not limit them by modern methods of prophylaxis. A detailed study of the prevalence of dysentery in individual localities strengthens this assumption.

Upon the appearance of dysentery in small cities or villages, almost all susceptible persons contract the disease, so that, in Japan, it is not unusual to encounter 5 to 10 per cent of the entire population of a village

attacked by the malady; but in this event, no cases, or at least very few, appear during the next following year, the epidemic entering the neighboring hamlets. If, on the other hand, dysentery, during the first year, appears only in the late autumn or early winter and if only a small number of people are attacked, then in the coming season a large epidemic, which, as a rule, will entirely disappear in the third year, must be expected. Reinfection, by which the disease is contracted in two successive years, is, according to my experience, of very rare occurrence. Among 10,000 patients sick with dysentery I have only observed such a recurrence in three or four instances and in these the first attack had been a very mild one. I have never observed a reinfection with patients in whom the course of the disease had been very severe.

The main factors in the spread of dysentery are the hosts (i. e., the individuals who convey the bacillus in the intestinal tract); and of these, three classes are to be considered: First, healthy persons; second, those who have mild cases of dysentery or of diarrhœa respectively; third, convalescent dysentery patients.

As is the case in typhoid, cholera, or diphtheria, perfectly healthy individuals may serve as hosts for the bacillus without manifesting a single symptom of dysentery, but to bring the proof of the presence of the bacillus in healthy stools is extremely difficult; however, Conradi succeeded in so doing in three cases which he encountered in a small epidemic of dysentery at Metz. During an outbreak of dysentery we often encounter patients affected with this disease or with diarrhœa, who clinically only show the symptoms of a simple intestinal catarrh but in whom dysentery can with certainty be demonstrated by bacteriologic methods and such cases appear not only in times of epidemics but also during the cold seasons. So-called winter diarrhœa often belongs to this category and in this way the bacillus is conveyed from person to person. I do not believe the organism can live for any length of time outside the human body. It maintains its existence therein throughout the winter and if it reaches the outside world during a favorable time in the early summer it may then cause a great epidemic. We were able to demonstrate the presence of the dysentery bacillus in stools which macroscopically had a perfectly normal appearance and which had been taken from patients one or two weeks after their convalescence. The fact that dysentery patients who were dismissed from the hospital as entirely cured would at times suffer a relapse after several weeks, or that the disease appeared in their respective families, would seem to prove that the bacillus can be present in the stools of convalescents for even a longer time than that given above; however, the question as to whether the specific organism can remain in the stools of convalescents for years, as is the case with typhoid, is still an open one.

Forster has lately emphasized the fact that the bacillus of typhoid finds a permanent habitat in the gall bladder, from which, from time to time,

together with the bile, it finds its way into the intestinal canal. Such an occurrence we have not as yet been able to prove in the case of dysentery. Dr. Amako in Kobe, made cultures from the bile and spleen of 16 cadavers dead of dysentery, but he never was able to demonstrate the presence of the bacillus and these experiments made the assumption probable that the organism of dysentery, unlike that of typhoid, can not find its way into the circulation.

TYPES OF DYSENTERY BACILLI.

The etiological importance of the dysentery bacillus as the causative factor in dysentery was first proven by Flexner [2] and by Strong [2, 3] in Manila, and the latter author, at that time, had already strictly distinguished between two types of dysentery—i. e., bacillary and amœbic. The latter type, as a rule, takes a chronic course and amœbæ, generally, can at all times be discovered in the stools, whereas the former is an acute disease the causative factor of which lies in the bacillus of dysentery.

Kruse,[4] in 1901, first called attention to the fact that an organism discovered by him in Germany is not entirely identical with the one observed in Manila. During an epidemic of dysentery occurring in a prison he encountered a second bacterium which differed from the Shiga-Kruse bacillus only in respect to its serum reaction; the latter organism he termed the pseudodysentery bacillus, and this variety was soon thereafter also discovered by Spronck[5] in Holland. Martini and Lenz[6] confirmed this observation of Kruse and even extended it, for Lenz[7] succeeded in differentiating the Shiga-Kruse stem from the Manila one by cultural methods, in that he demonstrated that the former did not, whereas the latter did, ferment mannite which he had placed in his culture media. Hiss and Russell,[8] independently of Lenz, but at the same time, showed that a bacillus, isolated by them from a case of infantile diarrhœa, and termed "bacillus Y," differed from the Shiga-Kruse stem in its fermentive action on mannite, and following this publication a further paper by Hiss[9] appeared in which the author separated the bacillus of dysentery, which he had isolated from patients attacked by dysentery and infantile diarrhœa, into three groups based upon cultures obtained on media containing, respectively, mannite, dextrose, maltose, saccharose, and dextrin. Gay[10] distinguished two groups of dysentery bacilli, founding his deductions on the bacteriolytic action of and the protection given by the immune serum, and finally Hiss,[11] using the fermentative action on the above-mentioned carbohydrates, succeeded in giving a reliable classification; and

[2] *Phil. Med. Journ.* (1900), Sept. 1, **6**, 414. Also *Bulletin of Johns Hopkins Hospital* (1900), Oct., **11**, 231.

[3] *Journ. Am. Med. Assoc.* (1900), Aug. 25, **35**, 498 and 501, also *Circulars on Tropical Diseases* (1901), No 1, Feb., Manila, P. I.

[4] *Deut. Med. Woch.* (1901), **27**, 370, 386, 637.

[5] *Baumgartnen's Jahresbericht* (1901), **17**, 473.

[6] *Zeit. für. Hyg. u. Infect.* (1902), **41**, 540.

[7] *Loc. cit.*, 540.

[8] *N. Y. Med. News* (1903), Feb. 14, **82**, 289.

[9] *Journ. Med. Research* (1904), new series, **8**, 12.

[10] *Univ. of Penn. Med. Bull.* (1903), **16**, 171.

[11] *Loc. cit.*, p. 1.

this action also accords with the agglutination phenomena and the absorbability of the agglutines. The following table gives his conclusions:

Group 1: Ferments dextrose only (Shiga, Kruse, Flexner's New Haven bacillus).

Group 2: Ferments dextrose and mannite (bacillus Y, Ferran, Seal Harbor bacillus).

Group 3: Ferments dextrose, mannite, and saccharose (Flexner-Strong Manila bacillus).

Group 4: Ferments dextrose, mannite, saccharose, maltose, and dextrin (Harris, Gay, Baltimore and Wollstein's bacillus).

The author, in conjunction with Ohno, has been working in Japan during the past year on the types of the dysentery bacillus. As many stems of this organism as it was possible to procure were sent from various regions and these were accurately investigated. At first we studied the power these organisms possessed of causing fermentation in mannite and other carbohydrates (dextrose, maltose, saccharose, dextrin, and lactose), following the methods laid down by Hiss, but, for the purpose of classification, we also took cognizance of four other properties—i. e., (*a*) indol reaction, (*b*) agglutination, (*c*) bacteriolysis, and (*d*) preventive action of the immune sera. The dysentery bacilli could be divided into three groups, if the indol reaction is to be taken as a criterion, as follows:

Group 1: Nonindol forming (Type I).

Group 2: Forming indol with difficulty (Type II).

Group 3: Forming indol with ease (Types III, IV, and V).

The third of the above groups forms indol with the greatest readiness in a 1 per cent aqueous peptone solution; the reaction appears promptly and very decidedly. The second does not form indol in this solution during one to two weeks, but gives a weak and inconstant reaction after three; however, in a 2 per cent culture a distinct reaction can be observed after the expiration of one week. The first does not form indol under any circumstances.

The fermentative actions of these dysentery bacilli on mannite and other carbohydrates are very complicated and somewhat variable. To judge from these phenomena, Ohno was able to distinguish sixteen varieties, among which were six which did not ferment mannite (so-called *non-acid bacilli*) and ten which did (so-called *acid bacilli*). (See Table II.)

The fermentation of dextrose and mannite is constant, but that of maltose, saccharose, dextrin, and lactose varies considerably both qualitatively and quantitatively, and so great is this variation that it seems to me impossible to give a correct classification based upon this property. Owing to this contingency, five groups, the fermentative properties of which could be distinguished with some certainty, were selected from the numerous subvarieties. (See Table III.) The first four groups in this classification accord entirely with those of Hiss, but in addition to these a fifth, which has not been differentiated by Hiss and other observers, has

been added. This type can be distinguished from the fourth one in that after twenty-four hours, it gives an acid reaction on a culture medium containing mannite but this gradually disappears until finally, after four days, the medium becomes alkaline and remains so. Therefore this type is a form intermediary between the acid and non-acid dysentery bacilli.

The agglutination phenomena of these five groups of dysentery bacilli on the whole agree with the fermentative action on mannite and the other carbohydrates. The rabbit yields a specific immune-serum against the different types of the organism, and therefore this animal is recommended for carrying on the experimental work; the goat, on the other hand, frequently does not give a specific immune-serum, and hence can not be employed to so great an advantage; and finally, the immune-serum to be obtained from the horse is useless for this purpose, as it generally gives an unreliable group reaction. Types I and V form the two end points in the agglutination phenomena; each immune-serum obtained by their use has a specific but no common reaction, or, in other words, neither one has agglutino-receptors common to the other. Types II, III, and IV show a gradual transition from one extreme to the other. (See Table IV.) The bacteriolysis brought about by the rabbit immune-serum is also not a strictly specific phenomenon, because the serum of one group frequently exerts more or less of an action on the others.

If all of the experiments outlined above are taken into consideration, it finally becomes evident that the total results of the fermentation of carbohydrates, the phenomena of agglutination and those of bacteriolysis are not only not entirely in accord but that they even are somewhat contradictory. Therefore, from the data at hand it seems to me impossible to arrive at a final classification, and consequently, lacking a better one, I will, for the present, retain the division into five groups which I have outlined; a discussion of another system arising from the standpoint of serum therapy will be entered into below.

THE OCCURRENCE OF SPECIAL TYPES OF DYSENTERY BACILLI ENCOUNTERED IN DIFFERENT EPIDEMICS.

As has been shown above, other varieties of dysentery bacilli (*para* dysentery bacilli) exist in addition to the one which was first discovered, and these forms, as well as the one originally described, are etiological factors in the causation of the disease, so that the important question as to the relationship between the first and the subsequent varieties was at once forced upon us. In order to find the answer, the occurrence of the various types of dysentery bacilli in their epidemological behavior was studied, to accomplish which end I obtained many cultures of the organisms from various provinces and countries and subjected them all to exact study. The bacillus which was first described by me was encountered in by far the greater percentage of cases among dysentery

patients in Korea, in the Japanese army in Manchuria, among the Russian troops in Port Arthur and the sailors from the ships of the Baltic fleet which had capitulated, but in the epidemic in Tokyo and some of the provinces of Japan the other varieties were met with in much the greater number of patients; indeed, the original bacillus was identified in only a few of the approximately 200 cases which occurred during the outbreak of the past year in Tokyo. Dr. Amako, in the same year, in an epidemic which raged in the city of Kobe, encountered a very interesting experience. In Kobe dysentery first made its appearance in July, at first with a few sporadic cases in different parts of the city, and in these the *varieties* of the original dysentery bacillus were encountered exclusively; however, in the beginning of August very large numbers of infections occurred in the western portions of the municipality and among these the original organism itself was almost the only one met with, and beginning with this time it was detected in dysentery patients in the most diverse districts of the city, so that subsequently, not only the original dysentery bacillus but also its varieties appeared side by side throughout whole sections of the city. After this time the infections with the original bacillus gradually diminished in number until, finally, toward the end of the epidemic the varieties were the only ones which could be observed. (See Table V.)

It is my opinion that the bacillus first described in 1898, the date when my investigations on dysentery were begun, was present in by far the greater number of cases, because, if this were not the case, I would have encountered many difficulties in its study, for at that time I investigated hundreds of cases of dysentery by bacteriological methods and in almost all I isolated from the stools of the patients the dysentery bacillus which I then discussed in the literature, its identification being chiefly by means of the agglutination reaction (for the greater part with rabbit immune serum). My original stem is the non-acid forming one, identical with Kruse's bacillus. This identity was entirely accidental. The bacillus discovered in Manila in 1900 by Flexner and by Strong is *acid forming,* but, on the other hand, the organism which was kindly sent to me from Manila by Dr. Strong in the past year, was *non-acid* forming and therefore it is likewise purely accidental that the acid-forming variety was first discovered in the latter city. In this connection the opportunity should be taken of mentioning cases in which the original bacillus as well as the varieties have been encountered simultaneously. Gay and Duval report three such instances in acute dysentery in adults, Hastings two, and finally Duval and Shorer six in the summer diarrhœa of infants.

Finally, the dysenteries which are caused by the varieties of the bacillus on the whole seem to take a milder course than those occasioned by the original stem, although a tolerably high mortality also occurs with the former, as will be seen from table.

In conclusion, a few experiments on the preparation of a curative serum, based upon work which has extended over more than a year, will be given. In a practical way these experiments are highly important, as the bacilli of dysentery occur in various types which, from the standpoint of methods of immunization, are considerably removed from one another. For technical purposes, were it possible, it would be highly desirable to prepare a universal serum which would be active against all of the dysentery bacilli, by the treatment of animals *with one type of bacillus only*. Unfortunately, this can not be done. We have already seen that the rabbit immune serum from each of the five is to a certain extent specific in its agglutinating and bacteriolytic properties, and it is therefore *a priori* highly improbable that a universal serum could be prepared by immunizing with one type only.

Horses react toward dysentery bacilli very differently from rabbits; thus, for example, the horse immune serum produced with the original type of bacillus is also more or less effective toward the others, but this group reaction is not sufficiently great to be of value for therapeutic purposes. In immunizing horses I have several times had unfortunate, but instructive, experiences. On one occasion, when the resistance of an animal was so high that it could well endure the injection of 25 agar cultures of Types I and II, it was given a similar dosage of Type V. Eight days thereafter it died of rupture of the liver. A second horse received 40 cultures of Type I and II and after fourteen days 45 agar cultures of Type V; thereupon the temperature rapidly rose to 39.4° and then quickly fell to below normal. The animal died from collapse three days after the injection. These observations seem to show that the treatment with Types I and II did not protect against Type V.

After this disgression I will once more return to my principal subject. After I had first shown that the immune serum of the horse, prepared either with the original bacillus or one of the varieties, was not active against all types, I continued the work with the purpose of ascertaining if a universal serum could be obtained by combining the immunizing properties of the original type and one of the varieties. For this purpose I immunized a number of horses with different combinations of dysentery bacilli and then tested the immune serum with the different types.

The method of testing was as follows: Diminishing quantities of the serum were added to the cultures of the dysentery bacilli in five times the fatal doses, and the resulting mixtures injected intraperitoneally into mice. A fixed quantity on an accurately calibrated platinum oese was taken from an incubated twenty-four-hour agar culture, suspended in an accurately measured quantity of normal salt solution so that 1 cubic centimeter contained exactly 2 milligrams of bacilli. The immune serum was added to test tubes in the following quantities: 0.5, 0.25, 0.1, 0.05, 0.025, 0.01, and 0.005 and all of the tubes were filled to 1 cubic centimeter, after which 1 cubic centimeter of the suspension of the bacilli was added; 0.4 of this mixture was then injected intraperitoneally into each of two mice of 12 to 14 grams weight. As one-fifth of the mixture in the tubes had

been injected in each instance, then the serum in the individual doses was as follows: 0.1, 0.05, 0.025, 0.01, 0.005, 0.0025, and 0.001. The result was taken after twenty-four hours.

It is necessary to remember that dysentery bacilli very rapidly lose their virulence, so that, after some weeks' standing they are already not appropriate for the purpose of testing sera; however, I have succeeded in maintaining their virulence successfully during more than one year by placing the cultures of the strains in the refrigerator immediately upon their isolation. When they are to be used some of this culture is retransplanted to agar.

A few examples of my numerous experiments with different sera are given below. (See Table VI.) The third type of the bacillus is lacking in this table, as the cultures which I had at my disposition had already lost their virulence and were therefore no longer available for animal experiments, but I have shown in other instances that Type III is acted upon almost as well by serum from Type II as is the latter bacillus itself. As the table demonstrates, the serum from Type I more or less affects Types IV and V, that from Type II feebly acts upon Type I, and is almost without effect upon Types IV and V, but, on the other hand, Types IV and V are closely related to each other, so that a serum from one of these acts almost as well upon the other as it does upon itself.

The above experiments show that a universal serum can be obtained by mixing the immune serum secured from Types I and II with that from I and IV. It is true that if we take three horses and immunize one of them against Type I, the second against Type II, and the third against Type IV, and then mix the sera prepared from all three, we also would obtain a universal serum, but the disadvantages of this method would consist in the fact that the individual titer of each serum would be reduced to one-third of the value which it would have if it alone were present.

For the purpose of immunizing horses the alternating separate injection of cultures of two types is recommended. If a mixture of the two is used, serious suppuration at the point of injection generally takes place, with the result of greatly reducing the acquired immunity. It is also true that as high an immunity is not obtainable if the two types are kept separate but injected simultaneously on both sides of the animal as if they were given in alternate doses, because then the quantity of any one used would only be one-half of the total. It must also be borne in mind that horses are very susceptible toward the original type, whereas they can very well endure the varieties; therefore the immunization can be forced about twice as far with the latter as it can with the former.

Owing to these considerations my advice is as follows: To immunize two horses simultaneously, the one with Types I and II, the other with I and IV, as soon as a high immunity is reached, serum should be taken from both and mixed in equal quantities. By this means the best universal serum can be obtained.

MAP OF JAPAN
SHOWING THE PROVINCES
HOKKAIDO
HONSHU
NORTHERN
CENTRAL
WESTERN
SHIKOKU
KYUSHU
130
134
138
142
146
45
43
41
39
37
35
33
31

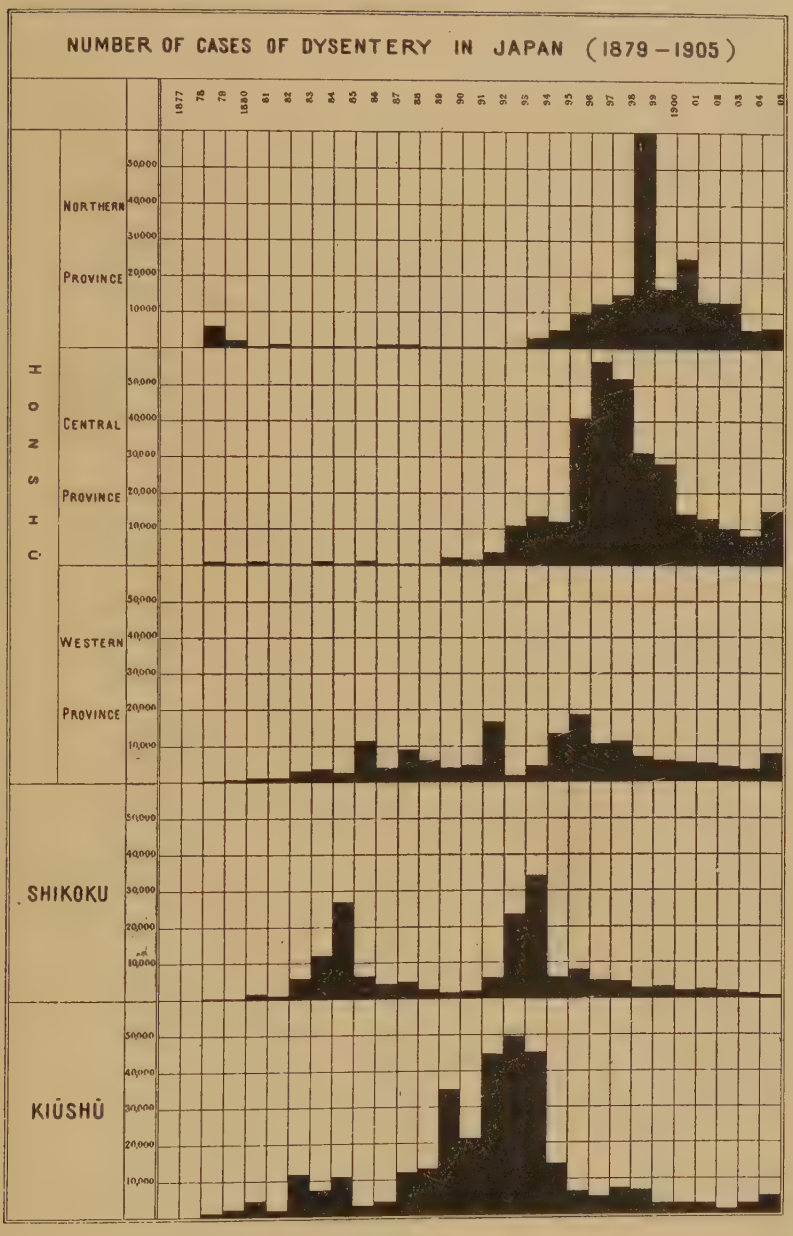
NUMBER OF CASES OF DYSENTERY IN JAPAN (1879–1905)
1877 78 79 1880 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 1900 01 02 03 04 05
CHŌSHŌ
NORTHERN PROVINCE
CENTRAL PROVINCE
WESTERN PROVINCE
SHIKOKU
KIŪSHŪ

TABLE I.

THE VARIETIES OF THE DYSENTERY BACILLI
(ACCORDING TO DR. OHNO).

	No	Dextrose	Mannite	Maltose	Saccharose	Dextrin	Lactose
Original Bacillus	1	+	−	−	−	−	−
	2	+	−	+	−	−	−
	3	+	−	−	+	−	−
	4	+	−	−	−	+	−
	5	+	−	−	−	−	+
	6	+	−	−	+	+	+
Varieties (acid-form)	7	+	+	−	−	−	−
	8	+	+	−	+	−	−
	9	+	+	+	+	−	−
	10	+	+	−	−	+	−
	11	+	+	−	+	+	−
	12	+	+	+	+	+	−
	13	+	+	−	−	−	−
	14	+	+	+	−	−	+
	15	+	+	−	+	+	+
	16	+	+	+	+	+	+

TABLE II.

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TYPES OF DYSENTERY BACILLI								
		INDOL	DEXTROSE	MANNITE	SACCHAROSE	MALTOSE	DEXTRIN	LACTOSE
TYPE I (ORIGINAL DYSENTERY BACILLUS)		—	+	—	—	—	—	—
TYPE II OR 1	VARIETIES	±	+	+	—	—	—	—
TYPE III OR 2	VARIETIES	+	+	+	+	—	—	—
TYPE IV OR 3	VARIETIES	+	+	+	+	+	+	—
TYPE V OR 4	VARIETIES	+	+	±	+	+	+	—

TABLE III.

DYSENTERY BACILLUS	RABBIT IMMUNE-SERUM				
	TYPE I	II	III	IV	V
AGGLUTINATION					
TYPE I	1600	-25	-25	-25	-25
" II	400	6400	3200	800	400
" III	-25	6400	6400	200	800
" IV	100	400	400	6400	800
" V	-25	100	400	1600	3200
	BACTERIOLYSIS IN VITRO				
TYPE I	0.0035	0	?	0	0
" II	trace	0.0035	?	0.01	0
" III	?	?	?	?	?
" IV	0	0	?	0.001	0
" V	0	0	?	trace	0.001

TABLE IV.

TYPES OF DYSENTERY BACILLI ENCOUNTERED IN KOBE IN 1905 (ACCORDING TO DR. AMAKO).						
	TYPE I	TYPE II	TYPE III	TYPE IV	TYPE V	TOTAL
JANUARY	0	0	0	1	0	1
FEBRUARY	0	2	0	3	0	5
MARCH	0	0	2	1	0	3
APRIL	0	0	0	2	0	2
MAY	0	3	3	2	0	8
JUNE	5	0	4	3	0	12
JULY	26	43	36	7	0	112
AUGUST	44	79	70	5	3	201
SEPTEMBER	23	53	38	3	6	123
OCTOBER	10	21	13	5	0	49
NOVEMBER	0	3	1	3	0	7
DECEMBER	0	0	2	1	0	3
TOTAL	108	204	169	36	9	526
MORTALITY	13.8%	13.2%	11.8%	8.3%	11.1%	12.3%

TABLE V.

TESTS OF THE POLYVALENT IMMUNE SERA FROM THE HORSE

IMMUNE SERUM FROM	ANIMAL EXPERIMENT	TYPE I	TYPE II	TYPE IV	TYPE V
TYPE I	TITER	0.001	0	0.01	0.05
	BACTERIOLYSIS	0.00035	0.001	0	0
	AGGLUTINATION	0: 1600	1:400	1: 1600	1: 200
TYPE II	TITER	0.01	0.001	0	0
	BACTERIOLYSIS	0.0035	0.00035	0	0
	AGGLUTINATION	1: 800	1: 1600	1: 800	1: 400
TYPE I AND II	TITER	0.001	0.0025	0.01	0.05
	BACTERIOLYSIS	0. 001	0. 001	0	0
	AGGLUTINATION	1: 200	1: 1600	1: 800	1: 400
TYPE I AND IV	TITER	0.01	0	0.001	0.0025
	BACTERIOLYSIS	0. 001	0	0. 0035	0
	AGGLUTINATION	1: 800	1: 200	1: 800	1: 100
TYPE I AND V	TITER	0.0025	0	0.0025	0.001
	BACTERIOLYSIS	0. 001	0	0. 001	0
	AGGLUTINATION	1: 200	1: 400	1: 400	1: 400

TABLE VI.

A CONSIDERATION OF SOME OF BAIL'S RECENT VIEWS IN CONNECTION WITH THE STUDY OF IMMUNITY AND A COMPARISON OF THE VALUE OF PROTECTIVE INOCULATION WITH AGGRESSIN WITH THAT OF VACCINATION IN PLAGUE.[1]

By Richard P. Strong.

(*From the Biological Laboratory, Bureau of Science.*)

One of the more important studies on the subject of immunity appearing during the past year, and one which has attracted a large amount of attention, has been that of Bail,[2] published in several recent numbers of the *Archiv. für Hygiene.* In the introduction to his first paper, after discussing the question of the relationship between bacteriolysis and immunity, he suggests that either the immunity which enters into the animal body in the process of obtaining a bacteriolytic serum represents a false immunity—i. e., not a true resistance against the disease itself, but only one against its cause in the particular form employed—or that in reality it represents a true immunity, the special nature of which, however, arises in something else than bacteriolysis, which is merely an accompanying phenomenon. He further calls attention to the fact that during almost eight years, experiments have been carried on with the expectation of being able to explain the non-infective power of an animal through the processes of bacteriolysis, but he points out that apparently the conclusion should be reached that the germ-killing properties of the body fluids are primarily without value in interpreting the actual processes of immunity. In support of his views attention is called to the fact that the rabbit, whose blood serum usually possesses a powerfully antagonistic action against the anthrax bacillus, is susceptible to the disease anthrax, while the fowl, whose blood shows the opposite properties, is insusceptible. He also alludes to the fact that while immune bodies against this affection could usually be demonstrated in the blood serum of other animals, the proof of a regular relationship

[1] Read March 3, 1906, before the third annual meeting of the Philippine Islands Medical Association.

[2] Oskar Bail: *Archiv. für Hygiene* (1905), **52**, 272; **53**, 275; **53**, 302. Also *Deutsche Medizin. Wchnschr.* (1905), **31**, 1471, 1788.

between the quantity present and the susceptibility of the particular animal in question has failed entirely. Thus, for example, the serum of the sheep often contained very small amounts of immune bodies, that of the rabbit very much larger ones, and that of cattle extraordinarily large quantities of these substances. However, all of these animals have a nearly equal susceptibility for anthrax.

Bail in addition, calls attention to the very significant fact that those experiments, performed with bacteriolytic serum in the test tube, in which in order to approximate the conditions encountered in the animal body the cells of fresh organs were added to the serum, revealed the interesting result that the bactericidal properties of the serum disappeared or were greatly diminished. A somewhat similar phenomenon had also been observed in hæmolysis by Von Dungern,[3] Wilde,[4] Hoke,[5] and others which was explained by these authors as being due to other processes. However, Bail insists that it is of little importance whether this ineffectiveness is conditional upon a failure of immune bodies or of complements, since the chief fact remains that the phenomenon of bacteriolysis is immediately suspended as soon as there exists in the test tube a condition somewhat similar to that encountered in the internal organs. In opposition to Von Dungern and Wilde he claims that there are many reasons why this process of bacteriolysis, which results in the test tube, must fail in the animal body, and he emphasizes the warning that, in every experiment, a careful consideration should be given to the results before the conclusion is reached that the bacteriolysis to be observed *in vitro* will explain the relationship which exists in the animal body. He also calls attention to the fact that in the case of anthrax it was soon shown that neither within the body of the naturally immune fowl nor in that of the artificially immunized rabbit did any process occur which resembled the bacteriolysis observed in the test tube with anthrax baccilli and immune serum, nor did an anthrax protective serum from another animal possess any bactericidal properties against this organism. Therefore, he reasons that the idea of the possession by an animal of a blood and serum with bacteriolytic powers being looked upon as the reason either for its artificial or natural immunity against anthrax must be abandoned. Bail admits that, after a certain time, the death of the inoculated organisms must take place in the body of an immune animal, but he maintains that this process is the result not so much of the action of the body fluids, as of that of certain cells, particularly those of the bone marrow, and that it is not, as is the case where serum in a test tube is used, a quick one in which large numbers of bacteria are killed but on the contrary a relatively slow process accompanied by a

[3] V. Dungern: *München Med. Wchnschr.* (1900), **57**, 677.

[4] Wilde: *Berl. klin. Wchnschr.* (1901), **38**, 878; *Archiv. für Hygiene* (1902), **44**, 1.

[5] Hoke: *Centralbl. für Bakteriol.* Orig. (1903), **34**, 692.

gradual diminution of the organisms. In addition, he concedes that the observations outlined above were formerly considered to be of value only in regard to anthrax, but he argues that since the certainty of bactericidal immunity in anthrax formerly seemed to be generally accepted, that now, from its failure in this disease, doubt was thrown upon the value of bacteriolysis in other infections—for example, in typhoid and cholera. The author refers to the further work of Hoke,[6] who in an extensive series of experiments with different bacteria, demonstrated that when the bacteriolysis was performed in the test tube in such a manner that the conditions approximated the relationship which existed within the organs of an animal, the natural germ-killing power of rabbit serum either was greatly diminished or was entirely eliminated; and further, that after the addition of cells of organs to an entirely fresh serum, not only as in the case of anthrax did the action of the immune bodies fail but that of the complements as well. If, argues Bail, the bacteriolytic action of normal serum against the typhoid bacillus according to these experiments occurs with such difficulty in the rabbit's body, then just as little as in the case of anthrax can the natural bacteriolysis possessed by the blood of this animal against this bacterium be considered as the reason for the natural resistance of the rabbit against typhoid infection; and also, since according to the generally accepted opinion, the development of artificial immunity in typhoid depends only upon this definite tendency toward an increasing bacteriolytic power in the body fluids, then this power must either behave in a manner entirely different from the bacteriolytic one of normal serum, or it also can not be regarded as a reason for the explanation of the immunity. However, it has from the first clearly been shown that no difference in action between the two could be demonstrated, at least in test-tube experiments.

Bail next compares the phenomena of resistance and of immunity and cites experiments in which by the injection of bouillon, of different bacilli, etc., into the abdominal cavity of guinea pigs, insusceptibility against a number of different organisms was obtained. An exudate containing many leucocytes usually results from these injections and although Pfeiffer[7] has pointed out that such inflammatory effusions are rich in amboceptors which bind the bacterial receptors, Bail maintains that in such fluids the most marked, active process causing the destruction of the bacteria is not a bacteriolytic but a phagocytic one and that the bacteriolysis carried on outside of the cells is comparatively insignificant. In support of this statement he describes two experiments in detail. In the first, a guinea pig was given a small dose of cholera immune-serum subcutaneously and at the same time one of living cholera spirilla intraperitoneally. In the second, another animal received exactly the same

[6] Hoke: *Ztschr. für Heilk.* (1904), **25**, 197.

[7] Pfeiffer: *Kongress in Brussels, Pfeifferschen Referates ünd Schlussfolgerung*, **17**, 25. Ref. Bail, *Archiv. für Hygiene* (1905), **52**, 278.

inoculation as the first, but in addition 5 cubic centimeters of aleuronat was previously injected into the abdominal cavity. The second animal remained alive, and there was marked evidence of extensive phagocytosis in the abdominal cavity that did not occur in the case of the first animal, which died.

Bail assumes the position that this difference in behavior was dependent in the second case not upon an increased killing power of the fluids outside of the cells—i. e., upon bactericidal action—but that the resistance of the animal depended upon the degree of phagocytosis. He then describes experiments to show that,whereas the destruction of the typhoid bacillus under the proper influences may take place very quickly within the abdominal cavity of a guinea pig, within the organs of the same animal an identical result is certainly not observable.

In his further attack upon the significance of bacteriolysis, he points out that sera, such as were produced by Sobernheim in the treatment of animals with anthrax œdema and which showed high protective value, evidenced neither agglutinating nor bactericidal properties: whereas rabbits and large guinea pigs, inoculated subcutaneously or intraperitoneally for a long period with anthrax cultures grown at 42° C. or carefully killed, furnished sera which had a distinct if not very powerful agglutinating action (1–500), but, although *in vitro* their value in immune bodies was about three times this strength, they revealed no protective power for rabbits, even when the serum was injected at the same time with the bacteria. Moreover, the animal which furnished the best serum possessed no true immunity, since it succumbed within three days after a subcutaneous inoculation of less than 1,000 anthrax bacilli. Bail claims a somewhat similar relationship in typhoid fever and cholera, though he admits that there are certain differences with these diseases, owing to the fact that the cholera spirillum and the typhoid bacillus belong rather to the group of half, or facultative invasive, parasites for animals, or indeed, perhaps stand nearer to the saprophytes in contradistinction to the anthrax bacillus, which may be considered as a true invasive parasitic organism. He argues that when the above facts are all taken into consideration it is easy to understand why agglutinating and bacteriolytic sera may be obtained by the inoculation of an entirely avirulent cholera culture; since in this instance also we obtain immunity against the bacillus but not against the disease itself.

After insisting further upon the fallacies of the consideration of bacteriolysis in its relation to true immunity, many of the details of which can not be entered into here, Bail takes up the discussion of the "aggressins." As is well known, Kruse[8] originally particularly advocated the idea that, in their various relations with living tissues, pathogenic bacteria

[8] Kruse: *Beitr. zur path. Anat. u. z. allg. Path.* (1893), **12**, 333. See also Bail: *Centralbl. für Bakteriol.* Orig. (1904), **36**, 266, 397.

form chemical substances in their protoplasm which so act upon the cells and fluids of the animal for which the organism is pathogenic that they overcome its natural resistance against the infection. This author at first designated these substances as lysines, but, owing to the fact that this term came to be employed in a different sense, he together with Bail more recently proposed for them the name of "aggressins."

Bail also points out that a bacillus must injure and overcome the animal's natural protective power in order to survive in the body of an animal and produce its particular disease. This it is able to do by means of its aggressive properties, which depend upon a certain substance which may be designated as "aggressin." These aggressins he believes are only to be formed by the bacteria in the animal body and they are particularly to be encountered in pathological fluids such as œdemas and exudates which result from the inoculation of the different micro-organisms. Thus, anthrax aggressin is contained in the œdematous fluid resulting from the subcutaneous injection into animals of the anthrax bacillus, whereas in the exudate which forms in the abdominal or pleural cavity of the rabbit or guinea pig, following the inoculation of the typhoid bacillus or cholera spirillum, typhoid or cholera aggressin is met with. He maintains that when these different exudates were carefully centrifugalized and thus freed from all the animal cells and most of the bacteria, and were then sterilized, in each instance a clear, yellow fluid resulted which contained the particular aggressin. For these substances he emphasizes the following distinctions:

First. Non-lethal amounts of cholera and typhoid bacteria, when injected into the animal simultaneously with the corresponding aggressin, cause the death of the animal; that is, the aggressin stimulates the bacteria to the production of toxic substances in such quantities that the animal succumbs.

Second. Fatal doses of these bacteria, which, however, give rise only to comparatively mild or subacute infections, produce with the aid of aggressin very severe and acutely fatal ones; hence the aggressin must aid the bacteria favorably in their struggle against the animal during the course of the infection.

Third. By injections of aggressin into the abdominal cavity of animals, the protective action of a bactericidal serum may be suspended.

Fourth. By the injection of aggressin an immunity is obtained which differs widely from bactericidal immunity.

I believe Bail has by his extensive experiments undoubtedly demonstrated that results somewhat similar to those outlined in these conclusions occur for several infections, although it would appear that in typhoid fever and cholera his so-called aggressin immunity depends chiefly upon bacteriolysis. However, as I shall point out further on, the results of all of his work with these substances are apparently in great part dependent upon the action of and explained according to entirely different processes

from those he has outlined. Noteworthy among other specific qualities mentioned for the aggressins is the fact that heating for one-half hour at 55° to 60° destroys their action, while sterilization with chloroform, toluol, and dilute solutions of carbolic acid weakens it. Bail found that injections of aggressin alone were not particularly poisonous and never acutely caused death in animals. In case a fatal dose had been inoculated, there was always a prolonged illness with marked loss of weight. Not all of the exudates he produced contain aggressin an it was found to vary considerably in quantity in the different ones, but was usually likely to be present in largest amounts in the effusions which were rich in cells.

In his conclusions in regard to the aggressins he emphasizes the fact that their action can not be explained on the assumption of their being anti-complements or anti-immune bodies, soluble bacterial substances, free receptors, etc., but they must be considered as new substances which have heretofore been unrecognized and which are formed by the bacteria in the living organism during the course of the infection.

The great practical importance of Bail's observations, apart from their theoretical interest, can immediately be seen. Indeed, what he has maintained is that our ideas in regard to immunization with a number of different bacteria, and our method of obtaining immune sera, are erroneous; that in the production of such sera we have treated the animals merely with the bacteria or with bacterial products obtained in artificial and inanimate media, and not with the weapons by means of which the bacteria carry on the combat in the living body, namely, by means of aggressins. In this manner he claims sera to have been obtained which act upon the bacteria but not upon the aggressin, and he even goes further and states that a true immunity against the disease—that is, a really active serum—can only be obtained from the injection of the living organism under the influence of aggressin. In this manner, not an anti-serum against the bacillus but one against the aggressin, hence an anti-aggressin serum, is produced. Therefore, for the production of the true immunity he insists that the animal must be inoculated with aggressin—i. e., with the body fluids of an animal which has succumbed to the particular infection.

As has been mentioned, the work of Bail soon attracted the attention of other observers, and both Wassermann and Pfeiffer published articles relating to his studies. Pfeiffer and Friedberger, in their recent work entitled "Weitere Untersuchungen Ueber die Antagonistische Wirkung Normaler Sera," [9] have particularly considered the statement of Bail that, by intraperitoneal injections of an animal exudate containing aggressin into a guinea pig, the action of a bactericidal immune serum introduced at the same time could be entirely suspended. That such a suspension of the bacteriolytic process of an immune serum does take place within

[9] Pfeiffer und Friedberger: *Deutsche Medizin. Wchnschr.* (1905), **31**, 1145.

the abdominal cavity of an animal, when the bacteria which were tested were previously treated with normal serum of another animal, Pfeiffer and Friedberger had already previously shown.[10] In their most recent article they emphasize that this phenomenon can not be explained upon the aggressin hypothesis of Bail. They also show that it can not be elucidated upon the assumption that, when the normal serum is added to the bacteria, soluble substances, the free receptors of the organism, are taken up by the serum; and moreover that its action does not coincide with the theory of Sachs of complement deviation, which was suggested for the explanation of what at first appeared to be a similar process observed in hæmolysis.

Pfeiffer and Freidberger on the contrary believe that this antagonistic action represents the fundamental properties of a normal serum, and the subject therefore is one of very great significance in the processes of immunity. While it must be added that all observers do not accept their explanation for this phenomenon, notably among them Gay,[11] who believes that the explanation lies in the fact that specific serum-precipitates which are able to fix alexine are present, nevertheless it seems entirely clear that the process can not be satisfactorily explained according to the aggressin theory of Bail. Wassermann and Citron[12] in their paper have considered the question which is apparently of most practical importance in its relation to Bail's studies, namely, whether in the infected organism, in the conflict between the invading bacteria and the cells of the host, a substance, aggressin, actually is formed, and whether this in reality is a new substance and one which, as yet, we have not been able to demonstrate in our investigations of the living bacteria outside of the body.

As Wassermann has remarked, if this is the case then the further conclusions of Bail must be acknowledged, namely, that by means of aggressin an anti-aggressin serum can be obtained which will possess different qualities from those sera previously obtained by other methods and which, perhaps, may act against the infection in a more favorable manner. Wassermann and Citron first performed experiments relating to this subject in exactly the same manner as Bail had recommended and found that they could confirm his work. They next investigated the question as to whether these substances, termed aggressins, were to be found only in the living organism as a result of the infection. Their experiments were performed with typhoid, hog-cholera, and swine-plague bacilli. Sterile exudates produced in rabbits by the injection of aleuronat were collected in glass vessels in an aseptic manner and their sterility proven. The living bacteria were then added to the exudates and were placed in an incubator at 37° for twenty-four hours. The mixtures were next centrifugalized and the clear fluid drawn off from above and sterilized.

[10] Pfeiffer und Friedberger: *Deutsche Medizin. Wchnschr.* (1905), **31**, 6.
[11] Gay: *Centralbl. für Bakteriol.* Orig. (1905), **39**, 603.
[12] Wassermann und Citron: *Deutsche Medizin. Wchnschr.* (1905), **31**, 1101.

These exudates, after this treatment, showed exactly the same aggressin action as those which were produced by the occurrence of the infection in the living animal. Similar experiments were now performed with rabbits' normal *blood* serum to which the bacteria were added (*in vitro*), the mixtures being further treated in the same way. These sera also showed properties similar to those of the aggressins. Finally, the bacteria were merely suspended in distilled water, thoroughly shaken, sterilized, and separated by centrifugalization from the fluid; the watery extracts which were thus obtained and which contained the soluble substances of the bacteria also possessed exactly the same action as did Bail's aggressin exudates. Therefore, Wassermann and Citron conclude that the so-called aggressins of Bail have nothing to do with the living animal organism and that they are not new bodies but merely dissolved bacterial substances, with the immunizing properties of which we have long been familiar.

Shortly after the appearance of his first paper, Bail and his pupils and associates published further articles demonstrating that high and undoubted immunity could be obtained in animals by the inoculation of these so-called aggressin exudates. Bail demonstrated such results for typhoid, cholera, and anthrax infection, while Kikuchi [13] showed that by the use of dysentery aggressin guinea pigs could be immunized against infection with dysentery bacilli and rabbits against the action of the dysentery toxin. Still more important were the results obtained by Weil [14] in the immunization of animals against chicken cholera with aggressin exudates. The difficulties in obtaining active immunity against hæmorrhagic septicæmia have for a long time been well recognized. Inoculations with attenuated, living cultures have proved to be very unsatisfactory and Voges,[15] using killed cultures, obtained unfavorable results. However, Kitt,[16] who employed the œdematous fluids from animals dead of the affection, had better success. The production of a protective immune serum for this disease has also been difficult; indeed, several observers have maintained that hitherto a method of obtaining such a satisfactory serum has not been known. However, with the exudates containing aggressin, collected from the pleural cavity of animals infected with chicken cholera bacilli, Weil was able to immunize other animals and to obtain a protective immune serum of high potency. He points out that the action of this serum is not bacteriolytic but that it possesses anti-aggressive properties. As intimated, Weil's experiments

[13] Kikuchi: *Archiv für Hygiene* (1905), **52**, 378. *Ibid.* (1905), **54**, 297. See also the articles of Von Hoke on "Aggressive wirkung von Pneumokokken und Staphylokokken Exsudat," *Wiener Klin. Wchnschr.* (1905), **18**, 348, and *Ztschr. für Hygiene* (1905), **50**, 541, and of Salus "das Aggressin des Colibacterium," *Wiener Klin. Wchnschr.* (1905), **18**, 660.

[14] Weil: *Archiv. für Hygiene* (1905), **52**, 412. *Ibid.* (1905), **54**, 149.

[15] Voges: *Ztschr. für Hygiene* (1896), **23**, 149.

[16] Kitt, Kolle, und Wassermann: *Handbuch d. pathogenen Mikroorganismen* (1904), **4**, 969.

have also demonstrated that, by the injection of the aggressin exudates into animals, a higher immunity against chicken cholera resulted than had been obtained by any other method.

However, hardly three months ago, Citron,[17] working in Wassermann's laboratory, published experiments which showed that with sterilized aqueous extracts of the hog-cholera and swine-plague bacillus, he was also able to obtain a similar immunity in animals and to produce an immune serum which was of equal value with and which acted in a manner exactly similar to an anti-aggressin serum. He points out that the aggressin immunity is therefore not an immunity *sui generis*. Finally, in the last paper to appear from Hueppe's Institut (in which laboratory all the work of Bail and his associates has been carried on), the announcement is made by Hueppe and Kikuchi[18] that successful results have been obtained in the immunization of guinea pigs against plague infection by repeated inoculations with exudates containing plague aggressin. The experiments which are related briefly are very few in number, but the authors mention that in this paper it is their intention merely to call attention to the priority of the use of this method of immunization of animals against plague.

Up to the present time we were aware of no other reasonably sure method of immunizing guinea pigs against plague infection except by that one in which the living, attenuated plague bacillus was inoculated. Upon this subject I have recently reported in detail in the PHILIPPINE JOURNAL OF SCIENCE.[19] From numerous experiments on animals I had found that the living, attenuated plague bacillus caused higher immunity than the dead cultures of this organism in any form. However, while the method of *vaccination* was by far the most favorable one for practicable immunization, it could not perhaps, be said to be absolutely satisfactory from an experimental standpoint, because the *single* inoculation of a large dose of an avirulent plague culture, of such attenuation that it is never capable of causing the death of an animal even in very much larger amounts, does not invariably protect the animal against subsequent plague infection. Thus, with monkeys, from 60 to 80 per cent of the different series of those vaccinated with such a culture possessed high immunity and survived a subsequent inoculation of a multiple lethal dose of the virulent pest bacillus, but the remaining 20 to 40 per cent were not thoroughly immunized by the single vaccination and succumbed to the subsequent injection of the virulent organism. By using more virulent cultures for vaccination a higher percentage of animals was protected. However, in order thoroughly to immunize a greater proportion of the monkeys, it was necessary to use cultures of such virulence that

[17] Citron: *Centralbl. für Bakteriol.* Orig. (1905), **40**, 610.
[18] Hueppe und Kikuchi: *Centralbl. für Bakteriol.* Orig. (1905), **39**, 610.
[19] Strong: *Philippine Journal of Science*, (1906), **1**, 181.

some of the animals succumbed from the result of the vaccination itself—i. e., they died of a true plague infection, hence the limit of safety had been passed. Naturally, only cultures which were invariably non-fatal for animals could be employed or recommended for use in human beings, and with these cultures it has been possible to render immune, by a single inoculation and a moderate dose, only from 60 to 80 per cent of the experimental animals.

Therefore, when the announcement was made that, by immunization with repeated doses of aggressin, guinea pigs could also be protected against plague infection, the importance of this claim was readily appreciated, and I determined to convince myself of the value of this method and at the same time to discover if guinea pigs, perhaps the most susceptible of all animals to plague, could not be immunized with certain bacterial extracts of the plague bacillus, particularly since the method of immunization with animal exudates as it is recommended by Bail can not be considered practicable for the inoculation of large numbers of people. In this connection it may be mentioned that by experimental work I had already found that an extract of the plague bacillus obtained in a manner similar to that already employed in this laboratory in the manufacture of our cholera prophylactic [20] from the cholera spirillum was not sufficiently potent, since not over 40 per cent of the animals inoculated with large doses thereof proved to be fully immune. I therefore determined to modify this method and to employ such means as would injure the chemical substances of the plague bacillus as little as possible during the process of extraction. For this purpose a procedure similar to that suggested and used by Wassermann [21] for the purpose of obtaining immunizing substances from typhoid and hog-cholera bacilli, and employed in a modified manner by Brieger, Bassenge and Meyer,[22] was chosen.

Cultures of a strain of the plague bacillus of the highest obtainable virulence were grown upon the surface of large test tubes of agar during forty-eight hours at 30° C. The growth was then suspended in distilled water, 1 cubic centimeter of water being employed for each 30 milligrams of bacteria (a very concentrated suspension). The resulting mixture was then placed in a sterilized bottle and fastened upon an electrical shaking machine and thoroughly shaken for five days. At the end of this time it was removed and heated at 44° to 45° C. for one

[20] Strong: *American Medicine* (1903), **6**, 272; *Publications Biological Laboratory, Bureau of Government Laboratories* (1904), **16**, 1; *Journal of Infectious Diseases* (1905), **2**, 107.

[21] Wassermann und Citron: *Deutsche Medizin. Wchnschr.* (1905), **31**, 1102.

[22] Brieger: Sonderabdruck aus den *Verhandlungen des deutschen Kolonialkongresses* (1905), Sektion **2**, 182; also Brieger und Meyer, *Deutsche Medizin. Wchnschr.* (1904), **30**, 980; Bassenge and Meyer, *Centralb. für Bakteriol.* Abt. 1 (1904), **36**, 332.

hour, for the purpose of killing the remaining living bacteria; 0.5 per cent of carbolic acid was then added in order to complete the sterilization. After standing twenty-four hours the fluid was centrifugalized for five hours at a velocity of 4,000 revolutions a minute. The clear fluid above was then pipetted from the bacterial sediment.

The liquid obtained by this method is perfectly clear and amber colored, and, if the process has been carried on with sufficient care, it is sterile. Intraperitoneal inoculations into small guinea pigs of as large a dose as 5 cubic centimeters has in these animals in several instances produced convulsions which lasted for an hour or more but from which the animals have always recovered. It seems very likely that these symptoms owed their origin rather to the small yet appreciable amount of carbolic acid present, rather than to the extracted substances of the bacilli. A number of experiments have been performed in which *single* injections of this fluid in doses of from 2 to 5 cubic centimeters in guinea pigs and from 1 to 5 cubic centimeters in monkeys have been made. Since the development of pest immunity takes place slowly, the animals were not tested with the virulent pest organism until fifteen days after the injection of the fluid. In my last series of inoculations with such an extract, comprising fifty-three animals, none of the guinea pigs [23] and but 25 per cent of the monkeys, on subsequent inoculation with a virulent plague bacillus, proved to be immune. Therefore, the results in immunization with this extract of the plague bacillus in this series of experiments at least are not nearly as good as those obtained with the living organisms of sufficient attenuation to be used for human inoculation. Hence, immunization with the attenuated living plague bacillus must be acknowledged as being superior to that in which these extracts are employed, and therefore vaccination must still be considered

[23] The method employed in testing the immunity of the guinea pigs in these experiments was a severe one. The shaved abdomen of the animal was scarified with a sharp knife, three parallel incisions being made through the dermis. The abdomen in this region was then thoroughly massaged with a portion of a spleen of a guinea pig which had died a few hours previously of plague infection produced with a plague organism which had passed successively (without growth on artificial media) through over 150 animals. Portions of the *same* spleen which were known to contain very large numbers of plague bacilli were used for all the inoculations. The abdomen was scarified and the test thus made severe in order to demonstrate whether this method of immunization in which the extracted substances of the bacillus were employed was superior to that in which the living attenuated organism was used. However, these experiments are not to be considered as final in relation to the value of immunization with the free receptors of the plague bacillus as a further study of this subject with certain modifications of method, is at present being pursued. Moreover, having failed to immunize guinea pigs with single injections of this extract, I shall naturally now endeavor to demonstrate whether it is possible to immunize these animals with repeated doses, both of it and of the animal exudates such as Hueppe and Kikuchi employed.

the most satisfactory method for use in human protection against plague. However, my experiments have shown that with an extract of the plague bacillus I have been able to produce in monkeys a certain degree of immunity against plague infection, similar to that brought about by Hueppe and Kikuchi with peritoneal exudates from animals dead of plague, but since the extract I have obtained, while it exerts an action similar to that of the so-called aggressin exudates, is prepared by a different method, namely, from the bacteria which have been cultivated outside of the animal body and which have not been acted upon by an animal exudate, I shall propose to call it merely plague bacillus extract. In regard to the use of the term "anti-aggressin" for those sera obtained during the process of immunization against such diseases as anthrax, rinderpest, plague, etc., and in which diseases it has long been recognized that there is no true bacteriolytic immunity, it would appear that the previously proposed term of anti-infectious sera would answer as well if not better. The aggressins in spite of the work of Bail and his associates, must still be regarded as hypothetical substances.

A STUDY OF THE BLOOD IN DENGUE FEVER WITH PARTICULAR REFERENCE TO THE DIFFERENTIAL COUNT OF THE LEUCOCYTES IN THE DIAGNOSIS OF THE DISEASE.

By E. R. STITT.[1]

(*From the Laboratory of the United States Naval Hospital, Canacao, P. I.*)

Dengue resembles a composite photograph in that it is by adjusting and subordinating the symptomatology that one arrives at a diagnosis of the disease—the moment one symptom stands out preëminently, there is a strong probability of mistaking dengue for some other affection. In proof of this statement may be instanced a few cases which have been observed during the past six months and in which at first another disease had been diagnosed.

1. A case presenting unusually severe pains about the regions of the knees and wrists. This was diagnosed as acute articular rheumatism. A careful examination failed to show any swelling and the pain was more associated with the structures adjacent to it than with the joint itself. A rapid survey of the other, but less pronounced, symptoms, together with the blood examination, showed the case to be one of dengue.

2. A case where there was a gradual, step-like rise of temperature with an unusually heavily coated tongue and a marked right iliac tenderness. It was only when a most characteristic rash appeared and the temperature fell to normal by crisis that a correct diagnosis was made. It may be stated that negative agglutination caused this case to be very carefully studied, and it was in this connection that the blood changes, to which I shall presently refer, were first observed.

3. A man admitted to the hospital with a most profuse general rash, the case having been diagnosed as measles. From the standpoint of the rash it certainly resembled measles, but a marked *leucopœnia* with a rather characteristic differential count, together with the presence of less prominent symptoms, showed the case to be dengue.

4. Two cases in which there was an almost entire absence of eruption, but a history of previous malarial attacks, resembled æstivo-autumnal fever, but the negative evidence as to parasites and the striking difference as to blood findings, made the diagnosis easy.

In fresh dengue blood I have observed most suggestive vacuolation. There seems to be more of what might be termed a protoplasmic milkiness

[1] Read before the third annual meeting of the Philippine Islands Medical Association at Manila, March 2, 1906, by E. R. Stitt, M. D., surgeon and lieutenant-commander, United States Navy.

than is seen in vacuolation as it is ordinarily observed; furthermore, on several occasions I have been sure that I have seen movement, both amœboid and locomotor. Absence of staining reactions and constant watching have made me believe that I was simply observing vacuolar distortion from contraction of the red-cell stroma. I feel sure that an observer who has not repeatedly examined and carefully studied the unstained malarial parasite would in all probability mistake these vacuolations for *Plasmodium malariæ*.

While convinced of the great value of a differential count in the diagnosis of dengue yet, from practically negative findings in two undoubted cases of the disease, I should assign to it simply the place of a striking symptom and would not consider it to be a pathognomonic sign. For this reason it would seem advisable briefly to consider those symptoms which, in my opinion, are the most characteristic.

A valuable analysis of the symptomatology of the disease is to be found in the "Report of the Dengue Epidemic in Brisbane in 1905," [2] and in presenting my views as to the value of the various symptoms, I think I could not do better than briefly to discuss certain paragraphs in this report. Taking the symptoms in detail we have:

1. *Onset.*—This is stated to be sudden. This has been our experience, however, without any case of abrupt onset. There was always a period of several hours separating perfect health from manifestations of the disease. There was nothing approaching the case described by Martialis where one member of a family, who had up to that time escaped the disease, was seized in the midst of a pantomime in which he was mimicking the sufferings of the others.

2. *Temperature.*—This is stated to have ranged between 39° and 39.5° C. and most rarely reaching 40° or 40.6° C., it generally persisted as an initial rise during two or three days, and after a remission which, as a rule, lasted only for a few hours, it was followed by a terminal one continuing for one or two days and falling by crisis.

This has been exactly our experience with the fever, except that at times no remission was observed. Again, the fall by crisis almost always seemed to coincide with the maximum manifestations of the eruptions.

3. *Pains.*—In the report it is noted that post-orbital or frontal headaches were almost always present; that the eyeballs were generally tender to pressure and that lumbar pain was almost as common as the headaches. In addition, many patients complained of pains in the calves of the legs and in the regions adjacent to the joints but never in the joints. Our experience has been that, if we except the pains in the head and eyeballs, there has not as a rule been marked suffering, the patient experiencing more malaise than actual pain. Many of the cases have complained of a feeling as if sand were in the eyes.

[2] *Journ. Trop. Med.* (1905), **8**, 355.

4. *Nervous symptoms.*—In addition to the headaches, reference is made to other nervous manifestations such as insomnia and, particularly, depression during convalescence. This depression in our patients when we were assuring them that they were well of the disease, impressed us as a most striking symptom. In no disease, other than influenza, have I seen it so marked.

5. *The eruption.*—The initial eruption usually is reported to have been simply a blotchy flushing of the face and neck which disappeared rapidly. The terminal rash was present, or rather observed, in only about 50 per cent of the cases. It was stated to have been more like the rotheln or measles rash than scarlatiniform in character. This report refers to its predilection for the extensor surfaces of the elbows and knees and also to a carmine-pink suffusion of the palms and soles, which was regarded as being extremely characteristic.

In our cases the most striking feature of the eruption has appeared to be its early and marked appearance about the wrists, on which it was more abundant on the dorsal than on the flexor surfaces. I commonly describe it as the bracelet rash, having a wide, dorsal outline and a narrower ring of eruption underneath. We have frequently noted the rash on the palms of the hands, but it has seemed to resemble the erythematous syphilide of the palms more than what should be termed a suffusion. In only one of the cases was there an entire absence of secondary eruption; the patient being a Chinaman in whom the other symptoms and the differential count were quite characteristic. Stedman states that he has invariably failed to find the rash in dengue cases among the Chinese.

The symptoms described in connection with changes in the tongue, lymphatic glands, alimentary canal, renal and respiratory systems were so varied that little weight could be attached to them.

It is stated that early in the epidemic discussed in the above-mentioned report many of the cases were diagnosed as influenza and that in the absence of an exanthem in a patient presenting the symptoms of fever, muscular pains and great depression, the best means of diagnosing dengue was found to be in the almost entire absence of respiratory symptoms. It has certainly appeared to me in many respects greatly to resemble influenza.

Shortly after commencing my investigations as to variations in the percentages of the various leucocytes, I was greatly interested in reading a paragraph of an article by Surgeon D. N. Carpenter of the United States Navy [4] in which the author stated that he had found a most characteristic diminution of the polymorphonuclears and a corresponding increase in the small lymphocytes in the blood of dengue patients. This at once attracted my attention, inasmuch as up to that time I had almost

[4] Carpenter, D. N.: *Journ. Am. Med. Asso.* (1905), **45**, 982.

invariably noted a most marked increase of the large mononuclear leucocytes and transitionals, and almost an entire absence of small lymphocytes. The counts in five cases which had been very carefully studied averaged as follows:

	Per cent.
Polymorphonuclears	42
Large mononuclears and transitionals	40
Large lymphocytes	8
Small lymphocytes	8
Eosinophiles and mast cells	2

In all these cases the counts were made after the appearance of the rash, the patient having been sent to the hospital about the time of the terminal rash. Subsequently, a patient who had been admitted with dysentery developed a temperature of 39.5° C. on the second day after his admission. Suspecting dengue, a blood count was immediately made and recorded as follows:

	Per cent.
Polymorphonuclears	32
Large lymphocytes	25
Small lymphocytes	37
Large mononuclears and transitionals	6

After the appearance of the rash his differential count corresponded closely with the ones previously given.

As opportunity occurred to examine several cases at the commencement of the disease, we were surprised to find in one, during the first day of illness, a count of 50 per cent of small lymphocytes, with very few large lymphocytes and scarcely any large mononuclears. Repeated examinations were made daily in this case and the leucocytes were found to vary markedly from day to day, so that by the fourth one there were only about 8 per cent of small lymphocytes, the latter having been replaced by the large mononuclears and large lymphocytes.

When I refer to a small lymphocyte I mean the leucocyte which constitutes the characteristic element of lymphatic leukæmia and which is largely made up of nucleus, with only a narrow or crescentic fringe of cytoplasm. As a result of my limited experience I believe it to be very probable that, should differential counts be made in a large series of cases, it would develop that the diminution in percentage of polymorphonuclears is largely replaced, during the first day, by small lymphocytes, subsequently, the large lymphocytes would replace the small ones and on about the fifth day, or at the time of the appearance of the terminal rash, it would be noted that large mononuclears and transitionals had taken the place of the lymphocytes. It is this almost kaleidoscopic change in differential count which is so characteristic of dengue and I do not know of any other disease in any degree presenting such a striking variation.

It can readily be seen that the differential leucocyte count would be of very great value in the diseases which might specially be confounded

with dengue. In typhoid it is the rule to have a more or less constant increase in the percentage of the small lymphocytes, while in malaria we are all familiar with the fact that there is a large proportion of large mononuclears. In dengue we have at different periods the characteristics of these two diseases.

The blood has invariably shown a leucopenia, the counts varying from 1,450 to 5,280 per cubic millimeter. This fact, together with the differential count, would easily differentiate scarlet fever and measles.

From the beginning it was my aim in studying the blood of dengue to discover the bodies described by Graham of Beirut.

It will be remembered that this author claimed to have discovered a non-pigmented protozoön in the blood of patients suffering from dengue. He stated that it was constantly changing its position in the blood cell and that it increased from day to day so that by the fifth or sixth one it would be more than one-half the size of the red cell, and diagrammatically he represented it as at times projecting from the cell like a pseudopod. He stated that he was unable to stain these bodies. He also claimed that he found oval and spherical spores in the stomach and salivary glands of culex, these spores appearing forty-eight hours after the mosquito became infected. I have repeatedly and for extended periods searched blood specimens without finding anything which might be termed peculiar. As previously stated, I was struck with the remarkable vacuolations observed in fresh specimens.

My method of work was from time to time to examine fresh specimens, carefully ringed with vaseline, until crenation was so general as to be confusing. Any peculiarity of the red or white cells was noted, and specimens of the blood which were stained in three ways were carefully examined to verify such supposed findings. Films were stained with Wright's blood stain, hæmatoxylin, and eosin, and with thionin. In not a single instance could I find anything which would suggest a protozoön. Occasionally, I also employed prolonged staining with Wright's stain according to the method suggested by Castellani as a substitute for Giemsa's stain as used for *Spirochaeta pallida*.

While I did not have an opportunity to verify Graham's findings in regard to the mosquito, yet there are certain observations which would tend to strengthen his claim that the disease is transmitted by a species of culex. Every case of dengue sent to the Naval Hospital at Canacao has been treated in the wards, yet not once has there been an instance of infection among the large number of non-immunes who were present in the hospital. When the hospital was located at Cavite, it was commonly noted that practically every case admitted became infected with dengue while under treatment for the original complaint. During the present small epidemic in Cavite it has been observed that newcomers, sleeping in Cavite, were frequently infected. Since the admission of our first case in October, 1905, there has been a noticeable freedom from the mosquito pest, so much so that recently, even after carefully searching

the wards, it has been impossible to secure a single one of the insects for examination.

A very striking instance of freedom from attack while on board ship (where mosquitoes are generally rare), and infection when detailed for shore duty for only five days at Cavite, is given by Medical Director Persons, United States Navy, in the case of a squad of marines from the U. S. S. *Baltimore*. Twenty out of twenty-four marines, who had been ashore, contracted the disease after returning to the ship, while there was a total absence of infection among those who had remained aboard.[5]

As to the possibility of a micrococcus being the cause of dengue, as claimed by two investigators in 1885 and 1897, I am unable to give any evidence. However, this matter was investigated and reported upon negatively by the Government Laboratories of the Philippine Islands in 1902.[6] Of one thing I am convinced and that is that the disease is not infectious in the same sense as is influenza.

The claims of Eberle[7] that he found a "dengue plasmœbic organism" which was more minute and more active than the malarial parasite, I do not consider well founded. He states that the motion of the parasite is so swift, it appearing and disappearing so rapidly that, when shown to a microscopist, it is not apt to be seen. He describes and pictures in his diagrams sporulating bodies. The fact that he claims most satisfactory results in staining these bodies with weak eosin and methylene blue would indicate that in stained preparations their discovery should be one of little difficulty. The statement that he found phagocytes literally swarming with the minute organism of dengue (which was one-fifth the size of a red cell), and furthermore, an examination of this appearance in his diagrams, leads me to question whether he might not have been observing an aggregation of blood platelets. In many of my films stained by Wright's method I have seen masses of blood platelets which presented an appearance very similar to that pictured in Eberle's diagram. In conclusion I should consider the most characteristic blood findings of dengue to be the following:

1. Absence of a demonstrable protozoön.
2. Leucopænia.
3. Diminution of polymorphonuclears.
4. A striking variation in the percentage of other leucocytes at varying periods of the disease. At first a large increase in the small lymphocytes is observed, then the appearance of a greater proportion of large lymphocytes, and in the final stages (at the time of the terminal rash and during convalescence) a most striking increase in the mononuclears.

[5] Persons, R. C.: *Journ. Assoc. Military Surgeons* (1905), **17**, 324.

[6] Report of the Director of the Biological Laboratory from the *Annual Report of the Superintendent of Government Laboratories* (1902), 575.

[7] Eberle, H. A.: *N. Y. Med. Journ.* (1904), **80**, 1207.

CURVES SHOWING LEUCOCYTIC VARIATIONS IN DENGUE.

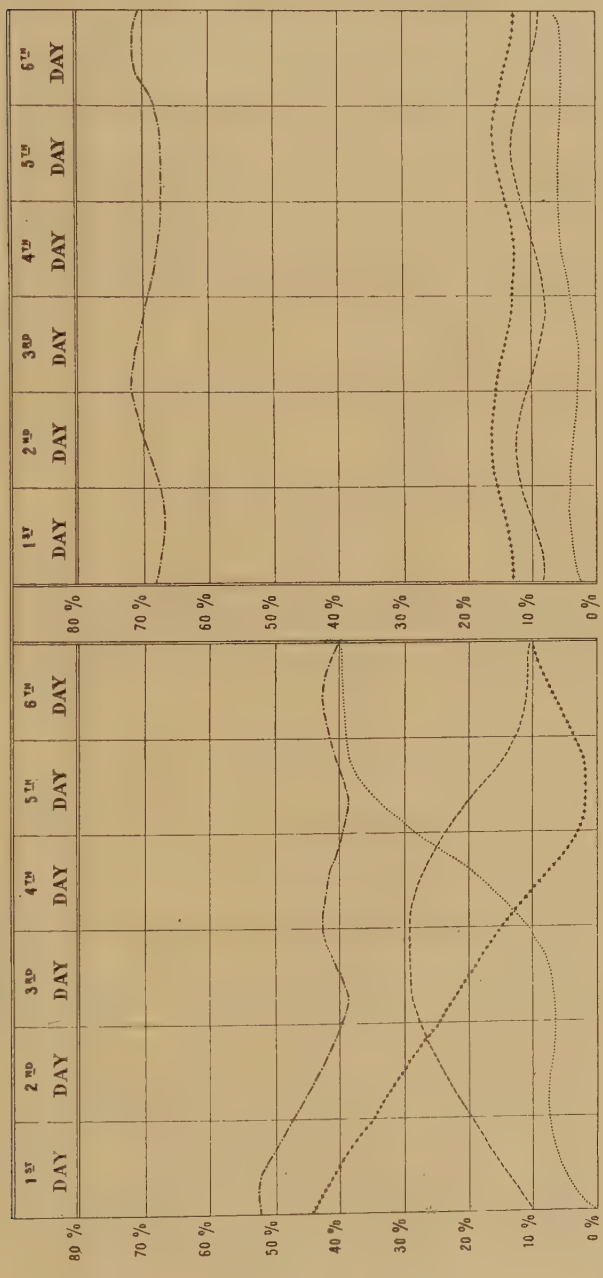

PLATE I.

CURVES SHOWING LEUCOCYTIC VARIATIONS IN DENGUE.

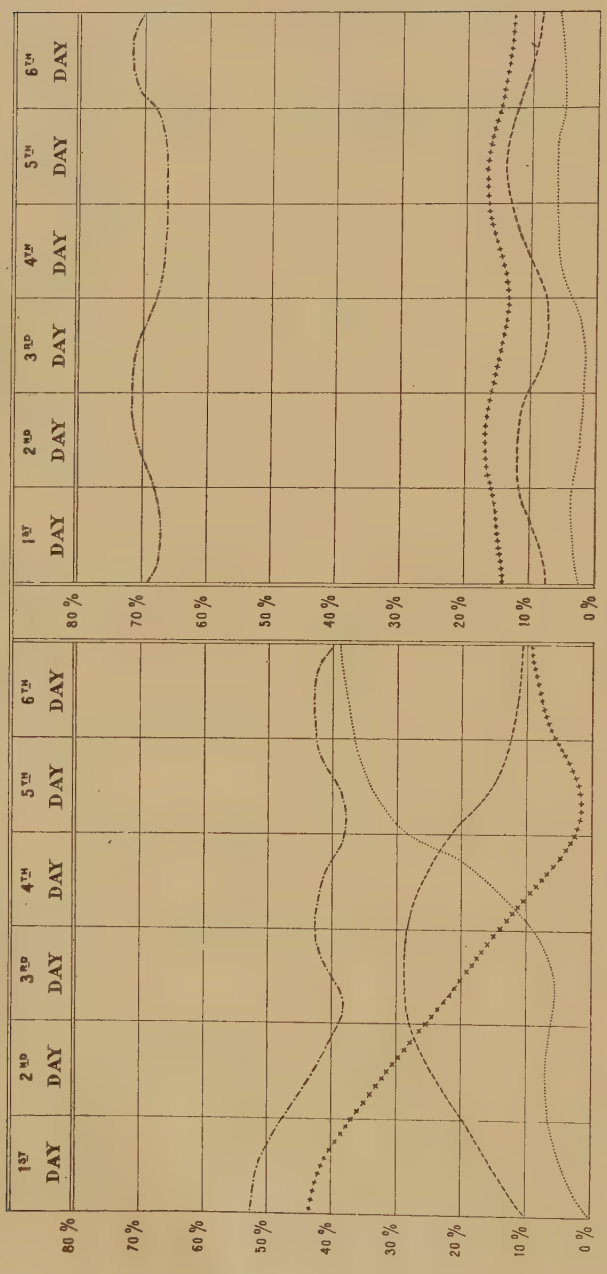

PLATE II.

CURVES SHOWING LEUCOCYTIC VARIATIONS IN DENGUE.

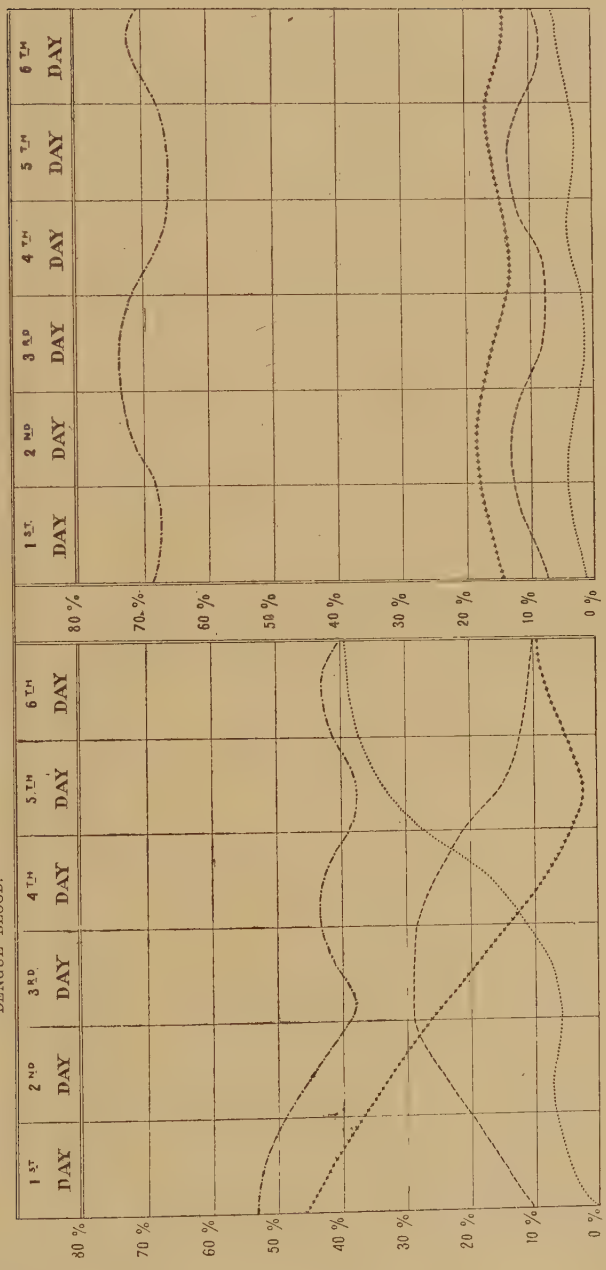

PLATE III.

CURVES SHOWING LEUCOCYTIC VARIATIONS IN DENGUE.

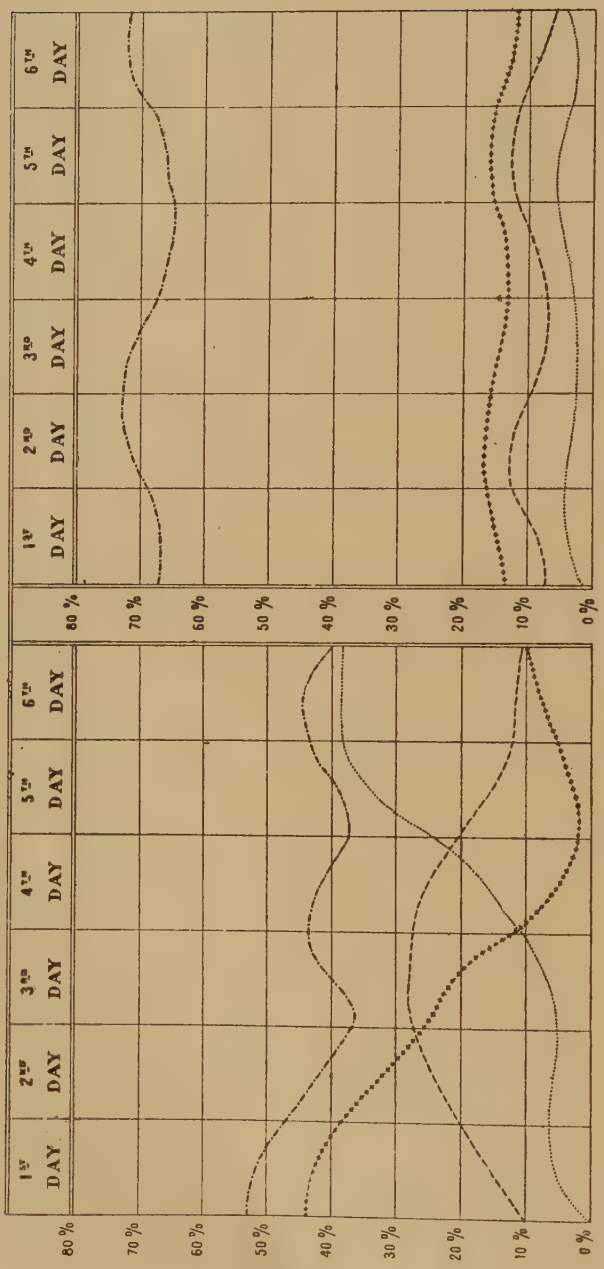

PLATE IV.

OBSERVATIONS UPON MALARIA: LATENT INFECTION IN NATIVES OF THE PHILIPPINE ISLANDS— INTRACORPUSCULAR CONJUGATION.[1]

By CHARLES F. CRAIG.

(From the Laboratory of the United States Army Hospital, Camp Stotsenberg, P. I.)

INTRODUCTION.

In this contribution it is my purpose to give in brief the results of some observations obtained upon malarial infections while I was on duty at the United States Army post at Camp Stotsenberg, Pampanga, Luzon, P. I.

The locality mentioned is one of the most favorable in the Philippines for the study of malaria, as cases of the disease are numerous in which all varieties of the plasmodium may be observed. The post is situated on the western border of the great Pampangan plain, near the Zambales Mountains, the station proper being placed in the foothills and at a considerable elevation above the plain. The soil is volcanic in nature, and even after the heaviest rains in a few hours becomes perfectly dry. There is no stagnant water within a mile, and therefore there are no breeding places of *Anopheles*. In order to reach the post these insects must travel at least one mile, and as they are at all times numerous it will be seen that in this instance the prevalent idea that they fly but a short distance is disproved. There is a considerable area of jungle country surrounding the station, some of which is situated within a radius of a few hundred yards, but I have failed, after the most careful exploration of these jungles, to find any breeding places of the *Anopheles* nearer to the post than one mile. It was invariably found that when the grass about Stotsenberg was allowed to grow to any great length the mosquitoes to a large extent increased, this being accompanied by a coincident rise in the number of cases of malaria; on the other hand, when it was cut, both mosquitoes and malaria diminished very appreciably.

[1] Read March 1, 1906, at the third annual meeting of the Philippine Islands Medical Association by Charles F. Craig, M. D., First Lieutenant, Assistant Surgeon, U. S. Army, member of U. S. Army Board for the Study of Tropical Diseases in the Philippine Islands.

Mosquitoes of the genus *Anopheles* are at certain times numerous while at others they are not to be found. During the latter portion of the rainy season the *Anopheles* begin to multiply, reaching their maximum during the months of November and December. This coincides with the increase in malarial infections at this post, as is shown in the following table:

Month.	Number of infections.	Month.	Number of infections.
1904.		1905—continued.	
August	24	April	10
September	57	May	14
October	24	June	17
November	58	July	11
December	75	August	29
1905.		September	31
January	76	October	43
February	27	November	54
March	20	December	126

During the five months in which I was stationed at Camp Stotsenberg I observed 386 cases of malaria in the blood of which I was able to demonstrate the parasite. Of these, 248 occurred in Americans and 138 in natives. As regards the type of infection, 98 were infected with the tertian plasmodium, of which 63 were Americans and 35 natives; 8 with the quartan, of which 2 were Americans and 6 natives; and 272 with the æstivo-autumnal plasmodium, 183 being Americans and 89 natives. Of the æstivo-autumnal infections, 258 were due to the tertian æstivo-autumnal plasmodium and 14 to the quotidian variety. There were 8 combined infections with the tertian and the æstivo-autumnal-tertian plasmodium.

The following table illustrates the character of the infections as regards their initial attacks:

Initial attacks, 227; in Americans, 227; in natives, 0.
Recurrent attacks, 38; in Americans, 18; in natives, 20.
Latent infections, 115; all in natives.

From a consideration of the data given above, several points of interest may be noted.

1. In regard to the type of plasmodium present, all varieties of malarial infection occur at Camp Stotsenberg, the æstivo-autumnal ones being the most numerous, the tertian next, and the quartan infections rare.

In the past there has been considerable discussion regarding which types of malarial infection were the most prevalent in the Philippines, and I have always maintained that here, as in almost all tropical regions, the æstivo-autumnal fevers are the commonest and certainly my studies at Camp Stotsenberg have only confirmed my belief. However, it must be admitted that the type of infection present in one locality can not be considered as a criterion in judging of that to be found in another. This is well shown by the fact that at Camp Gregg, 50 miles north of Stotsenberg, the prevailing malarial infections are tertian in character.

Admitting this, I am still of the opinion that the æstivo-autumnal is the prevailing type of malarial infection in the Philippine Islands.

In this connection, it should be remembered that the hyaline forms of the æstivo-autumnal plasmodia are the most difficult of any to demonstrate and therefore they are undoubtedly often overlooked, even by trained observers. Furthermore, it frequently requires repeated examination of the blood and a long and patient search to find them. It is perfectly evident when the data are carefully studied, that many, if not the majority of the so-called "simple continued fevers" which some medical men believe to be so prevalent in these Islands, are really unrecognized cases of æstivo-autumnal malarial infection.

2. Initial attacks of the malarial fevers are most common among the Americans, including in this term all whites. This would be expected, and it is not because of a relative immunity of the natives, for, as will be shown, such a relative immunity does not exist. It is due to the fact that a very large proportion of the natives in this locality are continually infected and suffer from relapses at longer or shorter intervals. It was but rarely that I was able to study an initial attack of malaria occurring in persons of the latter race and then it was only in very young children or in new arrivals.

3. Latent infections are most common in the natives, none being observed in Americans. However, in most of the latent cases a history of previous attacks of malaria could be obtained.

4. Recurrent attacks among the Americans were comparatively rare, due to the fact that every patient infected with malaria when treated in the hospital or in the post was required to take quinine once a week for several weeks and from our experience with this method there can be no doubt of its great efficiency in preventing recurrences of malarial infection.

LATENT INFECTION IN NATIVES OF THE PHILIPPINES.

The subject of latent infection in malarial disease more and more is receiving the attention which it deserves. We now know that an individual may harbor the malarial plasmodia for weeks or even months without suspecting that he is attacked, and during all of this time he may be a source of infection to others.

The observations of Koch, of Stephens and Cristophers in Africa, and of James in India prove that the greatest source of danger to the white man in a malarial locality lies in the native population, especially in the native children. The control of malarial infection in the Tropics will only be possible if quinine is issued to the native, and in the following observations it is my purpose to show that the latter race in the Philippines is the source of malarial infection. I will also attempt to show the futility of endeavoring to rid any locality of malaria so long as the native element in the question is neglected.

By a latent malarial infection we understand one in which the plasmodia of malaria may be demonstrated to be present in the blood of an individual, but in which no clinical symptoms of the disease of sufficient gravity to attract attention are to be observed. The term should not be confined to those instances in which no symptoms of malaria have ever been present, for in recurrent cases between the attacks, the disease is as truly latent as it is before the initial one. Under all circumstances the infected individual obviously is a great source of danger to others.

It appeared probable to me in considering the malarial situation as presented at Camp Stotsenberg, that the natives living in the barrios about the post were in all likelihood the chief source of infection, for while, as has been stated, the sanitary conditions in the post proper were such as to prohibit the belief that malarial infection could originate there, the same could not be said of the native barrios where the breeding places of mosquitoes abounded and insects of the genus *Anopheles* were numerous. In these situations the conditions for the spread of the human infection were ideal. In order to determine how large a percentage of the native population was infected, I made blood examinations whenever they could be obtained of all the natives living within 2 miles of the post. The results proved beyond question that the origin of malarial infection at Camp Stotsenberg is very largely due to the natives living in the immediate vicinity, and that any efforts to limit the disease must take this condition into account. In many of the persons of this race, the clinical symptoms of malaria were present at the time of the examination. Such cases are not included in this paper, which treats solely of latent infection in the native. In a considerable number of the instances of latent infection, even in the youngest children, a history of previous attacks of fever could be obtained, but in none of then were any symptoms of malaria observed at the time of the examination. In all, the blood of 225 natives was examined and 115 or 51.1 per cent were found to be infected.

James, in his work in India, found that the percentage of natives infected varied very greatly in different localities, being less than 5 per cent in some places and as high as 86 per cent in others. The same condition will be found to exist in these Islands and blood examinations of the natives will result in giving valuable data as to the endemicity of malarial disease in different localities in the Philippines. This factor should be considered and such blood examinations of the natives made before permanent military posts or residences are established in the Tropics.

Of the 115 infections found, the tertian plasmodium was present in 29, the quartan in 6, and the æstivo-autumnal in 77; of the latter, 73 were due to the tertian æstivo-autumnal plasmodium and 4 to the quotidian. There were 3 combined infections with the tertian and the tertian æstivo-autumnal plasmodium.

Latent infection in the adult native.—I was unable to examine the blood of more than 45 adults, of which 28, or 62.2 per cent, were infected; of these 5 were due to the tertian plasmodium and 23 to the tertian æstivo-autumnal variety. It is very probable that a further study of the blood of a larger number of adult natives would materially reduce this great percentage of infected cases, but from the above it is evident that the adult Filipino is more often infected than is the negro in Africa or the native of India.

Both Koch in Africa and James in India, have ascertained that the percentage of infected adults is very small. In the planting districts of the Duaro, James stated that he discovered no adults with plasmodia in their blood, although 65 to 75 per cent of the children were found to be infected.

Therefore, it is evident that the adult Filipino possesses little or no relative immunity to malaria, despite the fact that in malarial districts such adults have from childhood suffered repeated attacks of malarial disease. I have notes on several adult natives who, within two years, were admitted to the hospital from 8 to 16 times, suffering from attacks of malarial fever.

Latent infection in native children.—The blood of 180 children was examined, of which 87 or 48.3 per cent showed the presence of malarial plasmodia. Of these 34 were due to the tertian plasmodium, 6 to the quartan one, and 44 to the æstivo-autumnal variety; of the latter, 40 were infected with the tertian æstivo-autumnal and 4 with the quotidian æstivo-autumnal plasmodium. There were 3 cases which had the tertian and the tertian æstivo-autumnal plasmodium combined.

The infections in the children diminished in number with advancing age; thus, between the ages of one month and five years, among 40 children, 79 per cent; of 54 individuals between five and ten years, 37 per cent; and of 53 between ten and fifteen years 24.5 per cent of those examined were infected. These results agree with those of Koch, Stephens and Christophers, James and others, who invariably found that the younger the child, the more susceptible it was to malarial attack.

The following table illustrates the relationship between malarial infection and the age of the individual as observed in native children in the barrios about Camp Stotsenberg; it gives the number of children examined, the number attacked, arranged in five-year periods, the percentage of those infected, and the type of infection:

Age.	Number infected.	Per cent.	Tertian.	Quartan.	Æstivo-autumnal.
1 to 5 years 40	30	72.5	10	4	16
5 to 10 years 54	20	37	8	1	[a]10
10 to 15 years 53	13	24.5	5	1	7

[a] Combined, 1.

Only 146 children are considered in the above table because only in that number could the age be ascertained.

Family infections.—The malarial infections are strictly local, being confined within certain well-defined limits, even in infected localities. Thus Celli, in Italy, observed that the families living upon one side of a canal in a certain town suffered greatly from malaria, while those residing upon the other were practically free. This was very noticeable in the barrios about Stotsenberg, certain places in the barrios being badly infected while others were almost unattacked. Not only was this true, but it was observed that malarial disease was very largely a family one, certain families suffering severely while others were free. The following table illustrates the family character of malarial infection, being compiled from the data obtained in one barrio in which the families resided:

Family.	Number of members.	Number of infections.	Variety.
1	4	2	1, æstivo-autumnal; 1, tertian.
2	3	2	2, æstivo-autumnal.
3	4	2	1, æstivo-autumnal; 1, tertian.
4	5	4	2, æstivo-autumnal; 1, quartan; 1, tertian.
5	4	2	2, æstivo-autumnal.
6	3	2	2, æstivo-autumnal.
7	4	3	1, æstivo-autumnal; 1, tertian.
8	3	2	1, æstivo-autumnal; 1, quartan.
9	3	2	2, tertian.
10	6	4	2, æstivo-autumnal; 2, tertian.

In considering this table, it should be remembered that these infections are latent in character and I have repeatedly observed families in which every member was suffering from a malarial attack, some presenting the symptoms of the disease while in others the condition was latent. Such are Nos. 4 and 10 in the above table. Family No. 4 is of great interest because, of its 5 members, 1 was suffering from a severe attack of tertian malaria at the time I made the blood examinations, while of the other 4, 2 presented æstivo-autumnal, 1 the quartan, and the other the tertian plasmodium in the blood, so that in this one family all the varieties could be studied. From the data which has been given I believe it to be obvious that a large amount of the malaria at Camp Stotsenberg is directly due to the infection of the native, and there is no reason to doubt but that the same is true of every malarial locality in the Philippine Islands. The natives are the culture tubes holding the plasmodia, the mosquitoes the inoculating needles, and the "stranger within the gates" the victim of inoculation. It is also apparent that it is useless to expect to rid a locality, from which the mosquitoes can not be eliminated, of malaria, unless the infection is first stopped among the natives, and in the Tropics, where it is practically impossible to destroy all mosquitoes,

it appears to me that the greatest hope of success in combating malaria lies in the distribution of quinine. It would then make no difference how numerous the *Anopheles* might be, they would be harmless if the native were rendered free from the plasmodium by the use of quinine.

INTRACORPUSCULAR CONJUGATION.

In concluding these observations upon malarial infection I desire to call attention to intracorpuscular conjugation, a phase in the human life cycle of the malarial plasmodia, which I believe to be of the greatest importance, and which makes clear many obscure points in the clinical history of malarial infection.

This process was first mentioned by Mannaberg, but described more at length by Ewing[2] in 1901. Ewing concluded that, while conjugation of the malarial plasmodia undoubtedly occurred in the red blood corpuscles of man, it was by no means constant and probably of no essential importance in the human life cycle of the plasmodia. In a later contribution he states that the process may favor the multiplication of the plasmodia in the human host and that its disappearance tends to limit the malarial infection.

For nearly five years I have devoted much study to this process and have observed it in hundreds of cases. My results are given in detail in a recent publication[3] and at the present time I will only very briefly discuss the subject.

The process of intracorpuscular conjugation, as seen in the malarial plasmodia, is not a sexual act, for no difference in sex can be distinguished in the conjugating bodies. It is a process which is very common in many classes of protozoa and is intended to preserve the reproductive power of the organisms in which it occurs. By continued division, many of the protozoa eventually become exhausted and to prevent this result, conjugation occurs, the two conjugants, which are not sexually differentiated, becoming one, thus bringing about a restoration to former reproductive activity, due to a "rejuvenescence" of the vital activities of the organism. In what way this "rejuvenescence" results we do not know, but there can be no doubt but that if it were not for this interesting process many of the protozoa would cease to exist. In the case of the plasmodia of malaria, conjugation is a phase of the human life cycle and it occurs within the red blood corpuscles. It essentially consists in the permanent union of two hyaline ring forms, or hyaline bodies, is always complete before the development of pigment takes place and it occurs in all the species of malarial plasmodia.

The process may roughly be divided into three stages. In the first one the two hyaline rings are in contact, and in stained specimens it will be

[2] *Journ. of Exper. Med.* (1901), **5**, 429; *Clinical Pathology of the Blood* (1903), 454.

[3] Intracorpuscular Conjugation in the Malarial Plasmodia and Its Significance, *Amer. Med.* (1905), **10**, 982–1024.

noted that the chromatin of the nuclei in the two parasites is separate and that the union begins in the protoplasm of the organism. In the second stage, which may be designated as that of complete protoplasmic union, the chromatin masses become situated in the protoplasm of one organism which is formed by the union of that from the two. In the third stage, or the one of chromatic union, the two chromatin masses become united and form one large mass situated within the hyaline ring. Sometimes the union of the latter appears to be preceded by the loss of a small particle of chromatin from one of the masses. Briefly stated, intracorpuscular conjugation consists in the union, at some portion of the peripheral protoplasm, of two hyaline plasmodia, the two chromatin granules remaining separate; gradually the protoplasm of the two organisms unites, this union being followed by that of the chromatin masses and of the achromatic substance of the nuclei; conjugation is thus completed, the union being permanent and occurring within the erythrocytes.

The significance of the process.—Intracorpuscular conjugation is present in infections caused by all of the species of malarial plasmodia, namely, in the tertian, quartan, and æstivo-autumnal varieties. In order to understand the significance of the process it is necessary to observe in what type of malarial infection it occurs, whether or no it produces any peculiar clinical manifestations, and whether it is always present or is a rare phenomenon. From my studies, during which I have examined hundreds of specimens of blood from patients suffering from acute initial attacks of malaria, recurrent attacks and latent malarial infections with reference to this process, the following conclusions may be drawn:

First. Intracorpuscular conjugation is invariably present in every acute, initial attack of malarial infection, no matter whether it be due to the tertian, quartan, or æstivo-autumnal plasmodium. It is often difficult to demonstrate conjugating parasites, but repeated examinations will always result successfully.

Second. This process is present in the vast majority of instances of recurrent malarial infection caused by any of the species of malarial plasmodium.

Third. It is almost never present in latent malarial infection, the only cases in which it is noted being those which develop clinical symptoms within a day or two of the time of observation.

Fourth. The process of intracorpuscular conjugation has, in the vast majority of cases, a direct relationship to the severity of the clinical symptoms. When the latter are most severe, the number of conjugating plasmodia is greatest; in acute, initial attacks the conjugating plasmodia are always more numerous than in recurrent ones, unless the latter are of a severe character.

Fifth. The process is most easily observed in pernicious malarial infections, for in such the conjugating plasmodia are most numerous.

Sixth. This form of conjugation is not absolutely essential to sporulation or to the production of clinical symptoms.

Seventh. It is necessary for the maintenance of auto-infection, and its disappearance results eventually in spontaneous recovery of the patient.

As has been stated, conjugation in the protozoa is intended to prevent reproductive degeneration and to maintain the existence of the organism. In the malarial plasmodium the process is without doubt intended to preserve its reproductive power and all the facts which have been observed confirm this opinion.

Malarial plasmodia in man reproduce by spore formation, but a continuation of this process will ultimately end in exhaustion as it does with other protozoan organisms and such exhaustion is prevented by conjugation, after a certain number of generations of the plasmodia has been produced by sporulation. The result is a "rejuvenescence" of the nearly exhausted individuals and renewed activity in sporulation, and thus the malarial infection is maintained. In acute, initial attacks of malaria, conjugating plasmodia are always present, sporulating bodies are numerous and the clinical symptoms are pronounced. In latent infections, the first named are almost always absent, sporulating bodies are of very rare occurrence, and there are no clinical symptoms of malarial infection. During spontaneous recovery, conjugating plasmodia entirely disappear and if a relapse occurs they only reappear just before the occurrence of clinical symptoms. All of these facts point to but one conclusion, namely, that intracorpuscular conjugation favors the reproduction of the plasmodia of malaria, plays a very important part in the appearance of the clinical symptoms because it favors sporulation and its disappearance is the principal cause of spontaneous recovery.

TROPICAL FEBRILE SPLENOMEGALY.[1]

By Paul G. Woolley.

(*From the Serum Laboratory, Bureau of Science.*)

The disease known as tropical splenomegaly is characterized chiefly by splenic hypertrophy, emaciation, an irregular temperature uninfluenced by quinine and certain gastro-intestinal symptoms such as diarrhœa or dysentery. Christophers also maintains that amœbæ are invariably present. Such cases have been reported from various parts of India, from Egypt, China, Tunis, Algiers, Arabia, and the Philippine Islands.

Giles first considered the disease as a combination of malaria and anchylostomiasis and Bently thought it to be due to infection with *M. melitensis*. Rogers at first supposed it to be the result of a severe chronic malarial infection, but later in the cases from all of the above-mentioned sources save the last, a peculiar parasite has been described, first by Leishman in a case at Dum Dum in India, later by Donovan, Christophers, Rogers, Manson, Low, Phillips, Marchand, Ledingham, and others.

Since the publications of Leishman and Donovan, much speculation has arisen regarding the place which, in our classification, should be assigned to these parasites. Ross thought them to be an involution form of trypanosoma, and Laveran concluded that they belonged to the genus piroplasma or pirogma. Late investigations seem to point to the wisdom of Ross's conclusion, the weightiest reason being that Rogers has stated that in cultures of the bodies obtained by splenic puncture, after some days he has been able to demonstrate unmistakable trypanosomata which, to be sure, were very immature in most cases. Through the kindness of Dr. Strong I have had the pleasure of seeing some of Rogers's preparations, which were smears both from the spleen pulp and from cultures and while to judge from these it is not clear just what the relation of the two preparations is, nevertheless, in the cultures there were structures which very closely simulated trypanosomata. The Leishman bodies themselves were not especially convincing to me, perhaps because I have seen too few. However that may be, there seems to be a

[1] Read at the third annual meeting of the Philippine Islands Medical Association, March 2, 1906.

concensus of opinion in considering these bodies to be the causative parasites of *kala-azar*.

When present, these parasites are found in large numbers. They are difficult to distinguish in fresh specimens, but when seen can be differentiated from the platelets by their greater refractive power. They are most easily stained by the Romanowsky method or one of its modifications, and under these conditions their diameter is from 1.5 to 3.5 μ. They are usually circular or oval in form and often have a cockleshell appearance. They usually show two chromatin masses, a larger one which stains faintly and a small one which takes on an intense color. The former often is rod-shaped and the latter rounded, bilobed, or heart-shaped. They have been observed in the spleen, in intestinal ulcers, in the liver, mesenteric glands, bone marrow, kidneys, and in the skin in the disease known as Oriental sore.

It was in view of these facts and in the hope of being able to study these parasites that Dr. Musgrave, Dr. Wherry, and I began carefully to examine all cases of splenomegaly which we could find and control. The results of this study were published early in this year in the Bulletin of the Johns Hopkins Hospital.[2] In this paper we stated that splenomegaly was not infrequent in Filipinos, and that it was not difficult to find types corresponding with those of Osler (*Brühle*), Banti, and others. We then proceeded to describe some cases which apparently should be classed with the group of tropical, febrile splenomegaly.

These cases were characterized by the following symptoms: Splenomegaly, rheumatic pains, edema, diarrhœa with or without hepatic enlargement, and remittent fever. In none of these could malaria be found, neither was the course of the disease influenced by quinine, in none were the leucocytes above 8,000 (they averaged about 6,300), and in but one was the number of red corpuscles less than 3,000,000 per cubic millimeter. Unfortunately, at the time we made our observations we had no accurate means of determining the hæmoglobin, of which we have no record; however, it may be suspected from the appearance that there was some diminution. In five cases, splenic puncture was undertaken and in four of them examination in smears and cultures, and inoculation into guinea pigs and monkeys gave no result. In the fifth one there appeared in glucose-ascitic agar a faint growth of a small, coccus-like organism, which resisted transplantation.

In one of the seven cases which we reported the eosinophiles varied from 25.5 to 43 per cent, in another from 8 to 11.5 per cent; generally, the mononuclears were increased. The duration of the disease at the time of the last notes which we took was from three to fifteen years.

But one case has come to autopsy. In this instance the chief lesion consisted in a congestion, hypertrophy, and fibrosis of the spleen. Since the report of these cases another very interesting one has been brought to my attention, and for the opportunity of reporting it I have to thank Dr. Musgrave, from whose services in St. Paul's Hospital, Manila, it came.

[2] *Bull. Johns Hopkins Hospital* (1906), **17**, 28.

The patient was a Filipino *banquero*, aged 26, a native of Rizal Province. There was a past history of beriberi. He was admitted to St. Paul's Hospital suffering from ascites and splenomegaly, a condition which he said had been present for two months. He had an irregular temperature and a slight diarrhœa. (See chart No. 1.) His appetite was good. Blood examinations from time to time showed no malarial organisms, nor had quinine any effect upon his temperature. His urine showed a trace of albumen, and hyaline and granular casts. The stool examination was negative for parasites. Blood counts showed: Hæmoglobin, 80 per cent; red blood cells, 4,264,000; leucocytes, 5,400. A differential count showed polymorphonuclear leucocytes, 74 per cent; large morphonuclears, 10 per cent; small morphonuclears, 2 per cent; eosin, 11 per cent; cells, 3 per cent. From the time of his entrance into the hospital he had an irregular, remittent and intermittent temperature. He died a month after entrance. The clinical diagnosis was Banti's disease. Two days before his death a splenic puncture was undertaken and smears and cultures were made with the citrated material which was obtained. The smears showed a very small, polar-staining, rod-shaped or diplococcoid organism which was present in small numbers. The culture in glucose broth (+ 1 to phenolphthalein) after two days produced a powdery growth in the bottom of the tubes and a slight diffuse cloudiness. Agar cultures gave no growth. The autopsy was performed six hours after death.

Rigor mortis was present in the legs, feet, and jaws, but not in the anus. The pupils were normal. The lymphatic glands of the groins and axillæ were slightly enlarged and firm. Over the area of splenic dullness, a few centimeters from the midabdominal line and about a hand's-width above the pubis, was the puncture wound caused by the aspirating needle. The body was poorly nourished, the mucous membranes pale and slightly jaundiced. There were some pigmented scars on the shins, as there are in nearly all laboring Filipinos, but there were no periosteal irregularities. After opening the body, the point of entrance of the needle into the spleen could barely be seen, and about it there was no evidence of hæmorrhage or inflammation. The omentum was curled up along the transverse colon. The peritoneum was slightly dull in appearance and showed some points of injection. In the pelvis and flanks there was from 200 to 300 cubic centimeters of blood-stained fluid. The appendix apparently was normal. The left pleural cavity was obliterated by old adhesions. The right was normal. Both lungs were somewhat edematous and the seat of moderate hypostatic congestion.

The pericardium contained about 100 cubic centimeters of a clear, amber-like fluid. There was one large milk spot on the anterior surface of the heart. The myocardium was flabby and cloudy. The epicardial fat was somewhat increased in amount and along the auriculo-ventricular groove was a series of petechiæ. The cardiac valves apparently were normal. The auricles were filled with goose-fat clots. The liver weighed 750 grams and was very firm and resistant. Its surface was covered with nodular elevations varying in size from 1 to 5 millimeters. These elevations were of a greenish-yellow color in the center and were surrounded by zones of congestion. The cut section was granular and mottled yellowish-green and brownish. The increase of fibrous tissue, easily to be seen with the unaided eye, was diffuse. The gall bladder was small and contained no stones. The spleen weighed 1,770 grams and was firm in consistency. Its surface was smooth. It cut with increased resistance and the cut surface showed no tendency to diffluence. The increase in fibrous tissue was evident to the naked eye. The malpighian follicles were not noticeable. The kidneys were somewhat enlarged, pale and very flabby. The capsules were easily removed. The intestine contained liquid fæces with uncinaria and trichuris. In the large

intestine there were a few quite small, but rather ragged, superficial ulcers, surrounded by dark, pigmented zones. The submucosæ was œdematous and injected. The mucous membrane of the large bowel as a whole was somewhat œdematous and injected, that of the small bowel showed no change other than a catarrhal one. The mesenteric, intraperitoneal, and internal inguinal glands were markedly enlarged, and were, as a rule, pale, but with areas of congestion. The great blood vessels showed no abnormality. The pancreas was firm and pale.

Anatomic diagnosis.—Splenic hypertrophy; atrophic, hepatic cirrhosis; subacute, parenchymatous nephritis; abdominal, lymphatic, glandular hypertrophy; hypostatic congestion of the lungs; petechiæ beneath the visceral pericardium; persistent thymus.

At autopsy, cultures and smears were made from the spleen, liver, and heart. Those from the heart and liver showed no organisms. Those from the spleen gave a considerable number of small bacilli, similar to those found in the ante-mortem preparation. Cultures on glycerine, agar, and blood serum after forty-eight hours showed numerous discrete, minute, translucent, moist colonies. Transplants were made on various media with the following results: On alkaline and acid agar (1 per cent to phenolphthaleïn), glycerine, glucose and lactose, agar and blood serum, the organism in twenty-four to thirty-six hours gave rise to fine, almost transparent, moist columns, which increased but very little in size during the four or five days during which they remained alive. In glucose, saccharose, and inulin bouillon the growth was scarcely perceptible and took the form of a firm, flocculent precipitate, in which the organisms rapidly died out. Milk was acidified within twenty-four hours, coagulated in seventy-two hours, the caseïn separating from the whey in six days. On potato, the growth was not visible to the eye, but nevertheless it was present. The organism thrived best and lived longest in milk and in potato. It did not form indol. This organism, stained by Gram's method, is non-motile and pleomorphic, but when young and vigorous it appears as a very small, polar-staining rod. It ferments all of the sugars to a slight extent, without gas formation This was indicated by a change in acidity, which in the case of glucose required 0.2 cubic centimeter N/20 NaOH, in that of lactose 0.1 cubic centimeter, with saccharose 0.2 cubic centimeter, and inulin 0.25 cubic centimeter per cubic centimeter of the culture media, to neutralize. (The titrations were performed with phenolphthaleïn as an indicator.)

A monkey (*Macacus cynomologus*) was inoculated subcutaneously with 1 cubic centimeter of a suspension of the organism from an agar culture seventy-two hours old. A second monkey was inoculated in the same manner with 1 cubic centimeter of a suspension from a seventy-two-hour blood serum culture. The results, as far as the temperature was concerned, are shown by Charts Nos. 2 and 5. The organism used in the case of monkey No. 4 had been grown in blood serum for six generations. The constitutional symptoms were most marked in No. 1, which lost its appetite completely after a few days. This monkey was killed on the seventh day after inoculation. The spleen was not enlarged and the other organs showed no microscopic changes. Cultures from the blood and spleen were made upon agar, bouillon (—1 to phenolphthaleïn), and blood serum. No growth occurred in those from the spleen, but in the ones from the blood upon agar and blood serum a slight one occurred

in the water of condensation. One cubic centimeter of blood from this monkey was inoculated into another one (Chart No. 3), and 1 cubic centimeter of an extract of spleen pulp into a third (Chart No. 4). In monkey No. 1 the liver was much congested and there was a marked congestion at the site of inoculation. One cubic centimeter of a pure blood serum culture seventy-two hours old was also inoculated into a rabbit. No effect was produced and the animal is still alive and active. As the charts will show, monkey No. 4 died a month after inoculation, during which time it has had a very irregular temperature. Unfortunately, death occurred late in the afternoon and the animal was badly infected (post-mortem) when it was examined. The organisms with which it had been infected could not be isolated. The spleen was not especially enlarged. The other monkeys (Nos. 2 and 3) are still alive and will be closely watched.

Pieces of the tissues obtained at autopsy from the original case and fixed in Zenker's solution were imbedded in paraffin and sectioned. Sections were stained with carbol-fuchsin-gram-picro-indigo-carmin, methylene blue and eosin, hæmatoxylin and eosin, resorcin-fuchsin, Mallory's reticulum stain, and by Gram's method. The liver showed the usual picture of a well-marked mono- and multi-lobular cirrhosis with a slight degree of central cirrhosis. No bacteria could be demonstrated. The spleen section showed a marked congestion and a moderate degree of fibrosis which was especially noticeable in the immediate vicinity of the blood vessels. Atrophy of the malpighian bodies was also present. Sections stained by Gram's method showed clumps of small, polar-staining rods, scattered irregularly in the organ but chiefly noticeable in the more congested parts. None of these organisms were demonstrated either in the follicles or in the lymph glands.

If we compare these cases with those reported as *kala-azar* we see that, aside from the one point of absence of the Leishman bodies, a close analogy exists between them. Diarrhœa is a common feature in all of them. While, perhaps, amœbæ do not play a part in the causation of this symptom, yet, in the Tropics, other intestinal parasites are so frequent that we rarely encounter a native's stool free from one variety or another and frequently several may be met with simultaneously. In addition to the diarrhœa, the symptoms common to all of our cases were splenic enlargement, irregular temperature, transient œdemas, rheumatic pains, loss of weight and strength, and probably anæmia. Together with these, the liver may be enlarged or atrophic and there may be ascites. Of all of these symptoms the most important is splenomegaly. What is its cause?

In the Philippine Islands and elsewhere in the Tropics, malaria is an extremely common affection and its occurrence might explain the increase in the size of the spleen. However, in sections we do not find the evidence we should expect, for we encounter neither pigment nor parasites. Then, too, the irregular temperature in splenomegaly is not satisfactorily explained on these grounds, for quinine does not affect it. Another disease which we are beginning to consider a much more common

one than formerly is syphilis. But the assumption that the latter is present does not explain the temperature, for this is uninfluenced by mercury.

There remains the possibility of a chronic infection or intoxication originating in the intestinal tract. As we have seen, the bowel when symptoms of diarrhoea are present, in almost all instances is considerably damaged. In the last case described above, there were well-marked ulcers and in this and in others, trichuris and uncinaria occur. Is it not possible that the progressive cirrhosis of the spleen and liver is the result of continued absorption from the intestinal tract, aided by the increased permeability of the latter? It may be possible that the continuous absorption of toxins causes the cirrhosis and the penetration of bacteria produces the temperature variation. However that may be, it seems reasonable to assume that the condition may be explained upon the basis of intestinal absorption and that the condition of the intestinal walls may be the factor which determines the presence of a febrile or afebrile splenomegaly.

One striking feature of the symptom complex in the cases which we have examined is the sudden onset of the fever which resembles that of malaria or dengue.

I still believe, as I did after studying the first seven cases, that although a certain number of cases of tropical, febrile splenomegaly may be due to infection with the Leishman body, it will be necessary to search for further etiologic data before we can understand and satisfactorily classify the whole group of cases which are characterized by the general gross features of *kala-azar,* and I believe in all probability that there will be found associated with the clinical picture various organisms and that the symptoms will depend chiefly upon intestinal conditions and pathologic changes in the intestinal walls.

ILLUSTRATIONS.

[Photomicrographs by Martin.]

PLATE I.

FIG. 1. Section of spleen stained by Gram's method showing a focus of the organisms described. X 1000.

2. Same as fig. 1. X 1920.

PLATE II.

FIG. 1. The bacillus from a culture on glycerine agar, Gram's stain. X 1920.

2. The same organism, Gram's stain from bouillon culture. X 1920.

PLATE III.

FIG. 1. The same grown on potato during sixty hours. X 1920.

2. The same grown on blood serum ninety-six hours old. X 1920.

FIG. 1.

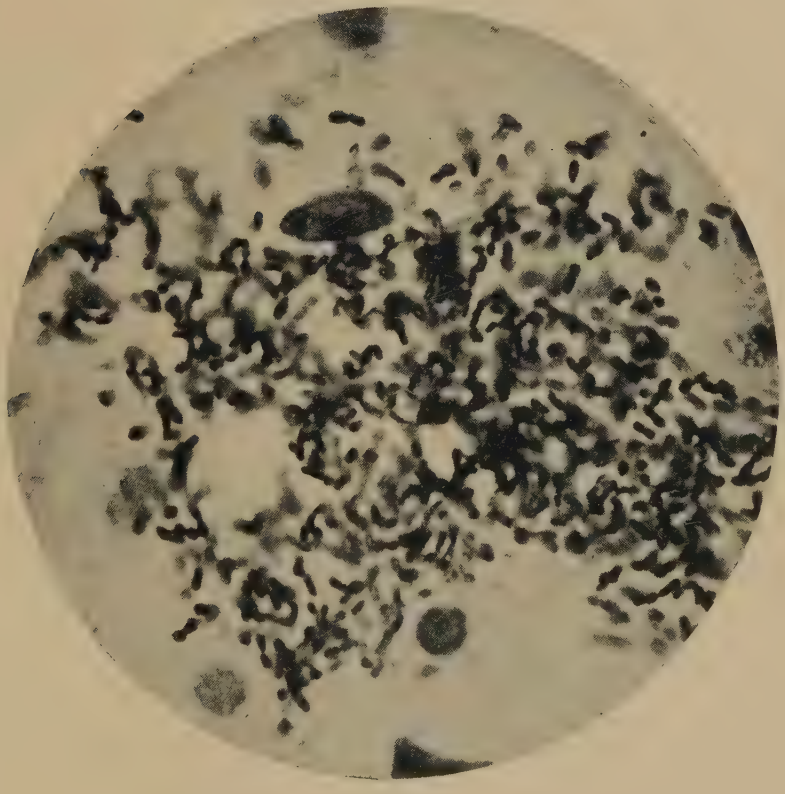

FIG. 2.

PLATE I.

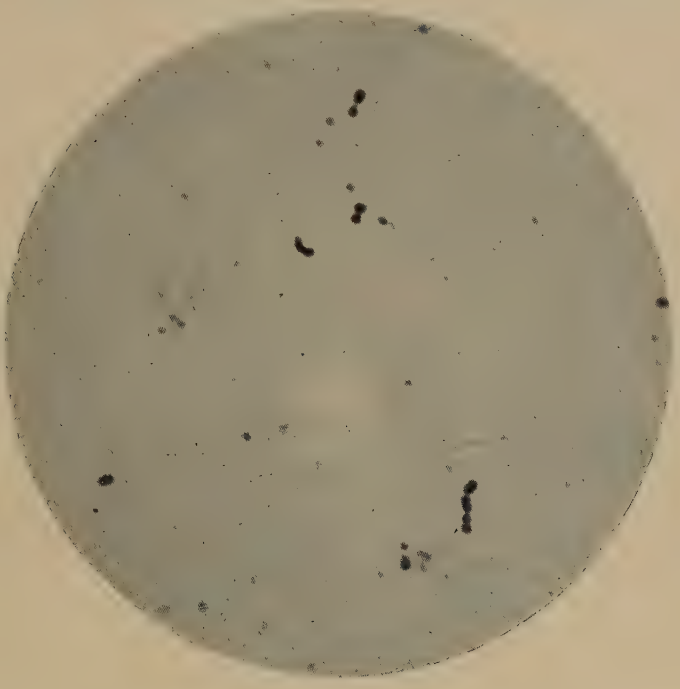

FIG. 1.

FIG. 2.

PLATE II.

FIG. 1.

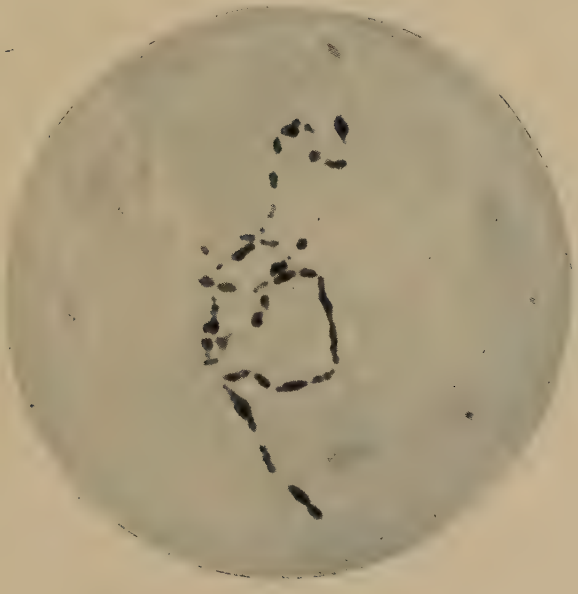

FIG. 2.

PLATE III.

No _____

November, 1905 Native Man.

Weight _____ Age 26 Sex M Color _____ Inoculation _____

History Bantí's Disease

TREATMENT	34	35	36	37	38	39	40	41	42	Date.	RESULTS
										16	
										17	
										18	
										19	
										20	
										21	
										22	
										23	
										24	
										25	
										26	
										27	
										28	
										29	
										30	
										1	
										2	
										3	
										4	
										5	
										6	
										7	
										8	
										9	
										10	
										11	
										12	
										13	
										14	
										15	
										16	
										17	
										18	

CHART NO. 1.

Monkey No. 1
December, 1905
Weight _____ Age _____ Sex _____ Color _____ Inoculation _____
History Inoculated with 1 c.c suspension of bacillus - Case of Banti's Disease

17470

TREATMENT	34	35	36	37	38	39	40	41	42	Date.	RESULTS.

CHART No. 2.

Monkey No 2
January , 1906
Weight _____ Age _____ Sex _____ Color _____ Inoculation _____
History Inoculated with 1 c.c. Heart's blood from Monkey "1

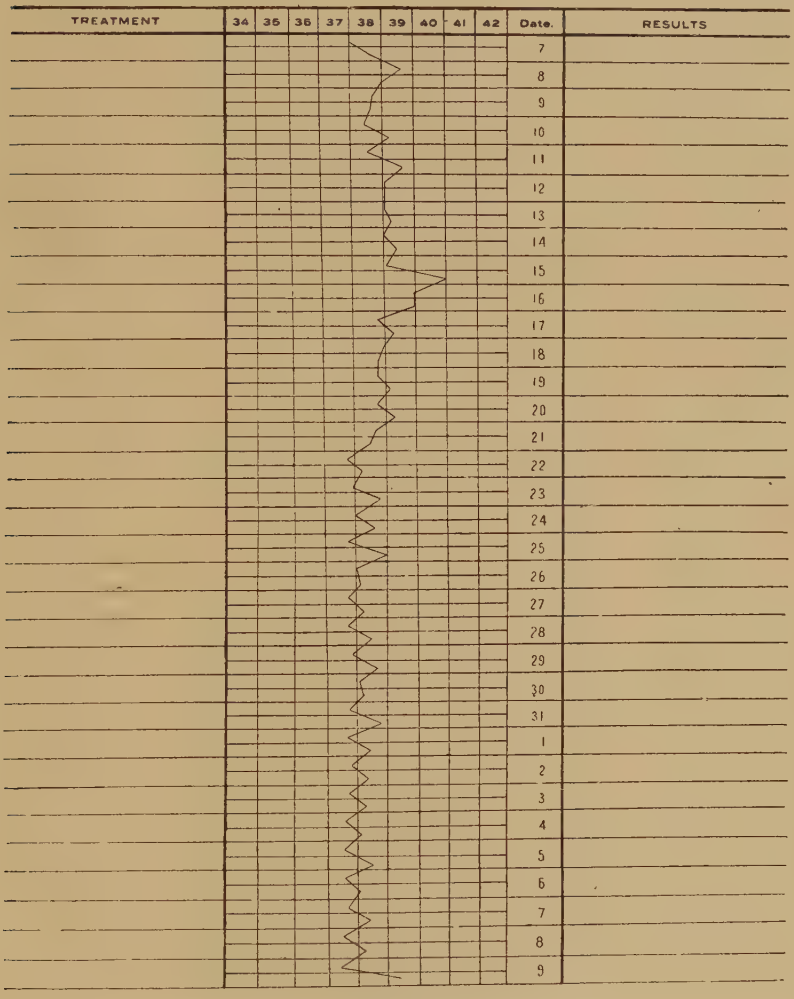

CHART NO. 3.

Monkey No. 3
January, 1906
Weight _____ Age _____ Sex _____ Color _____ Inoculation _____
History Inoculated with 1 c.c. splenic pulp Emulsion. Monkey "1

TREATMENT	34	35	36	37	38	39	40	41	42	Date.	RESULTS.
										7	
										8	
										9	
										10	
										11	
										12	
										13	
										14	
										15	
										16	
										17	
										18	
										19	
										20	
										21	
										22	
										23	
										24	
										25	
										26	
										27	
										28	
										29	
										30	
										31	
										1	
										2	
										3	
										4	
										5	
										6	
										7	
										8	
										9	

CHART NO. 4.

Monkey No. 4
January, 1906
Weight _____ Age _____ Sex _____ Color _____ Inoculation _____
History Inoculated with 1 c.c. 72 hr Blood serum culture in suspension

TREATMENT	34	35	36	37	38	39	40	41	42	Date.	RESULTS.
										17	
										18	
										19	
										20	
										21	
										22	
										23	
										24	
										25	
										26	
										27	
										28	
										29	
										30	
										31	
										1	
										2	
										3	
										4	
										5	
										6	
										7	
										8	
										9	
										10	
										11	
										12	
										13	
										14	
										15	
										16	Death.
Died										17	
										18	
										19	

CHART NO. 5.

AMŒBIASIS: ITS ASSOCIATION WITH OTHER DISEASES, ITS COMPLICATIONS, AND ITS AFTER EFFECTS.[1]

By W. E. Musgrave.
(*From the Biological Laboratory, Bureau of Science.*)

In this paper the more established facts concerning this subject will briefly be described, attention will be paid to points more or less neglected in previous publications and finally, certain new observations tending to elucidate some of the problems will be added. The subject may be outlined under the following headings:

I. Diseases and conditions accidentally associated with amœbiasis which do not modify the course of either infection.
II. Diseases of different etiology in which the association produces decided modifications in one or both.
III. Direct complications.
    (*a*) Of amœbic origin.
    (*b*) Of other parasitic or of bacterial origin.
IV. After effects of amœbic diseases.

I.

Complete discussion of the first heading would practically include the whole subject of tropical medicine, because amœbiasis in the Tropics is such a very common affection that almost every other disease has, at different times, been found associated with it.

Pregnancy, because of its frequent association with amœbiasis in females, is the only condition which will receive notice in this connection. Local treatment of the dysentery often increases the vomiting of pregnancy, but the danger of abortion from this cause is even less than that to which the untreated amœbiasis itself gives rise. Experience has taught us to give pregnant patients suffering from amœbic colitis the same thorough irrigations which are with confidence applied in other non-pregnant cases afflicted with this disease.

[1] Read March 3, 1906, at the third annual meeting of the Philippine Islands Medical Association.

II.

The second heading is of much greater importance and includes such diseases as malaria, beri-beri, Bright's disease, specific bacterial dysentery, tuberculosis, chronic rheumatism, certain nervous affections, and other diseases, some of which will also be duly considered under the third and fourth headings.

MALARIA.—This is far the most important disease in this second class. True malarial dysentery is recognized by many writers, but, entirely apart from this, the association of a simple, malarial infection with amœbiasis is very frequent, and the combination of the two makes each disease much more refractory to treatment than is either one alone. The symptomatology is also much modified and, in cases in which, in addition, liver abscess is suspected, the diagnosis is often very difficult. In these combined infections of malaria and dysentery, the treatment of the former affection alone often causes an improvement of the amœbic disease of the bowel, and quinine irrigations usually give satisfactory results in both, although obviously, in severe cases of malaria, the administration of larger doses of quinine is also advisable.

BERIBERI is endemic in the Philippine Islands and is frequently associated with amœbic and other parasitic infections of the intestine. Without questioning a specific, infectious etiology for beriberi, I would call particular attention to the favorable influence which treatment directed to the removal of intestinal parasites often has upon the course of the co-existent neuritis. Beriberi also exerts a bad influence on the amœbic infection, and if, as is claimed by some writers, changes are necessary in the intestinal wall before amœbæ can produce lesions, clinical and pathological observation would suggest beriberi as being one of the diseases in which such primary changes of the intestine would occur. M. Herzog, of this Bureau, has also called attention to this point in a paper read before the Manila Medical Society, February 8, 1906.

BRIGHT'S DISEASE.—Marked disturbance of kidney function, and even organic changes therein, may directly complicate the amœbic infection, and these will be discussed under the third heading, but, apart from this, there is the rather frequent association of established Bright's disease (of alcoholic or other etiology) with amœbiasis. Such a conjunction is a particularly difficult one to treat, because of the increased intensity of both diseases when combined, above that which would be expected from either alone. This increase becomes very pronounced in uræmia.

III. DIRECT COMPLICATIONS.

LIVER ABSCESS.—Amœbic abscess of the liver is of rather frequent occurrence in the Tropics and subtropics and is encountered sporadically in nearly all parts of the world. More than 95 per cent of all liver abscesses seen in the Philippine Islands are of this variety.

Frequency and association with intestinal amœbiasis.—Rogers collected 200 cases of amœbic liver abscess in examining 5,000 miscellaneous autopsy records in India. Among 10,603 patients (from American troops) in the Philippine Division Hospital it was diagnosed 34 times (Coffin). Strong and Musgrave encountered liver abscess 27 times in 400 miscellaneous autopsies performed, for the greater part, on American soldiers in the Philippines. In the first thousand patients, from a cosmopolitan population, admitted to St. Paul's Hospital, Manila, liver abscess was found in 12.

In the great majority of patients the abscess complicates an amœbic infection of the colon *and its frequency in this disease* is variously estimated as being from 5 to over 75 per cent of the cases. Councilman and Lafleur collected 486 liver abscess cases from the records of 2,430 autopsies on dysentery. Rogers found it in about 20 per cent of his large series; Strong and Musgrave in 23 of 100 fatal cases, mostly among American soldiers; Harris in 15 of 95; Futcher, in 27 of the 119 in the Johns Hopkins Hospital series; Craig in over 50 per cent of 3,210 collected cases and in 33.7 per cent of his own series; Coffin in 34 of 859 among American soldiers.

In the first 100 cases of amœbiasis treated in St. Paul's Hospital, of which 9 came to autopsy, it has been found 12 times. The diagnosis in each instance was made during life. It occurred 10 times in Americans and Europeans and twice in natives of the Philippine Islands.

In the great majority of cases the evidence that the abscess is secondary to amœbic infection of the colon is conclusive, but there are a number of instances in which it might appear to represent a primary amœbic infection of the liver, since the most careful search at autopsy fails to show any evidence whatever of a lesion of the bowel. Amœbic liver abscess is considered to be a distinct disease. That amœbæ could reach the liver in any other way than from the bowel seems improbable, and, if we admit this, there are then but three possible explanations of the *apparently* primary infection of the liver:

First. Amœbæ may reach the liver by the gall ducts.

Second. They may penetrate the bowel wall without producing apparent lesions; or

Third. The bowel lesions may have been entirely repaired.

The first of these propositions is untenable, because amœbæ have not been found in the gall bladder and ducts or even in the upper part of the intestine and, moreover, the undiluted bile is, at least in cultures, toxic for amœbæ. The second is a possible one, especially when we consider Schaudin's observations and the pathology of the early lesions of colon infection, as pointed out by several observers, and recently by Woolley and Musgrave.[2] However, the third furnishes the most satisfactory explanation, for it is well known that the process of repair, even in very extensive lesions of the intestine, is often so complete that no macroscopic evidence of the disease remains. In whatever manner the mode of entrance may be explained, the fact is fully established that amœbic abscess of the liver

[2] *Publications Biological Laboratory, Bureau of Government Laboratories,* Manila (1905), **32,** 31. Also *Jr. A. M. A.* (1905), **45,** Sept. 16 and Nov. 4.

may exist without *discoverable* lesions in the bowel *at the time of the death of the patient.*

Since my previous discussion which touched this subject,[3] one case of liver abscess has been encountered, in which the most careful and persistent search failed to give evidence of a previous dysentery, and there was no history of antecedent dysentery or diarrhœa. However, similar conditions and findings have occurred in other cases in which, some months before, there was a perfectly clear history of dysentery. Therefore, by taking everything into consideration, the conclusion is justifiable that the majority, if not all, of the cases of amœbic abscess of the liver in which, at autopsy, intestinal lesions were not discernible, occurred in individuals who had previously suffered with amœbic colitis, which had finally healed, and in which the amœbæ reached the liver during the period of active ulceration of the colon.

Relation of liver abscesses to the location of intestinal ulcers.—There does not appear to be any definite relation between the occurrence of liver abscess and the location of the intestinal lesion, or between it and the location of an intestinal perforation, should one occur, although the observations of several recent writers and my own indicate liver abscesses to be most frequent where there is ulceration of the cæcum and ascending colon.

In one series of 27 abscesses, 15 occurred without the perforation of the ulcers in the intestine; there were ulcerations in the cæcum and ascending colon in 8; in 1 in the transverse, and in 3 in the descending colon.

Again, in another series, we have perforations in the cæcum or ascending colon 9 times with 6 cases of liver abscess, and perforations in the descending colon 8 times with 1 liver abscess. In one series of 13 perforations of the intestinal ulcers, without liver abscess, 10 were below the hepatic flexure of the colon. In 11 solitary abscesses of the right lobe, the colon was ulcerated throughout in 6, and the cæcum and ascending colon alone in 5. In 2 multiple abscesses of the right lobe, the intestinal ulceration was general; in 8 multiple ones of right and left lobes, the entire bowel was ulcerated, and in 1 solitary abscess of the left lung, the transverse colon alone was found, at autopsy, to be ulcerated.

The location and the number of abscesses.—In over 90 per cent of all amœbic abscesses the right lobe is involved, either alone or in connection with other portions of the organ. It is the only one affected in over 70 per cent; and in 40 to 65 per cent of all cases the abscess is a solitary one. The most common condition by far, is a solitary abscess situated in the dome of the right lobe, and in this connection it must be remembered that solitary abscesses are not infrequent in the left lobe, less common in the *lobus spigelii* and that they occur only occasionally in the quadrate lobe. In rare instances, also, multiple abscesses have been confined to the left lobe, and once I have seen three small amœbic ones in the *lobus*

[3] *Publications Biological Laboratory, Bureau of Government Laboratories,* Manila (1904), **18**, 112.

spigelii alone. Although small abscesses are frequent and larger, solitary ones are occasionally seen in the deep substance of the liver, in the great majority of cases they are rather close to the surface, whichever lobe is involved. Sometimes, shallow abscesses several centimeters in diameter are situated between the dome of the liver and the diaphragm, but not extending more than 1 or 2 centimeters into the liver substance, the superior surface of such abscesses being entirely formed of a portion of the diaphragm. Twice I have seen very shallow, subcapsular abscesses of from 4 to 9 centimeters in diameter in other portions of the liver, one being situated on the inferior surface. Liver abscesses may vary in size from those having a diameter of 1 millimeter or less to the ones which fill almost the entire, involved lobe. My records include one in which the right lobe was only a shell, containing, at autopsy, over 4 liters of fluid.

Predisposing causes.—Age is a very important factor. It is true that amœbic abscesses have been reported in *children;* Amberg collected 35 cases of amœbic infection in individuals of this class, with 5 liver abscesses, and there have been several later reports confirming these results, but, at least in the Philippine Islands, it is of very rare occurrence. I have not encountered a case among a large number of children under 10 years of age who have been treated for intestinal amœbiasis, nor has one been found during several years of general post-mortem work in this country. Old age also seems to be somewhat protective, for my records show only one case in a man over 60 years of age. The disease is by far the most frequent in young adults and these records bear out the usual statement that males are much more often attacked than females.

Race seems to play an important part in the frequency of this disease. Several writers have noted the comparative infrequency of liver abscess in natives of the Tropics, and this is emphasized by the conditions in Manila. I have not seen an amœbic abscess in a Filipino. However, a few such cases have been observed by J. R. McDill, R. P. Strong, M. Herzog, M. T. Clegg and others in Manila. Intestinal amœbiasis is *very* prevalent among Filipinos.

The Chinese, owing, no doubt, to their excellent care in food and drink, are rarely sufferers from intestinal amœbiasis and, with my limited material, no case of abscess of the liver has been found among them.

Alcohol, in my opinion, has been given an overprominent place as a predisposing cause of liver abscess and although my statistics are not conclusive in this respect, it is certain that many cases are encountered among individuals who, without doubt, are non-alcoholics. The unacclimated are particularly liable to develop the disease and it is believed all will concede that very few persons drink less in their home countries and during the early days of their stay in the Philippines than they do later on.

The physical condition of the patient, the presence of associated disease, particularly of malaria, of the anæmias, and of other affections which are attended with intestinal autointoxication and with liver changes, naturally suggest themselves as predisposing factors, but definite and conclusive data are very difficult to obtain.

There are also other influences which are not fully understood and which may play a part as predisposing factors. Among these we must not lose sight of the condition of and the changes in the liver itself previous to infection. It may be stated without going more fully into the subject at this time that cultural experiments with amœbæ, now being carried on in this laboratory, indicate that amœbic abscess rarely or never develops in an otherwise normal liver, notwithstanding the fact that amœbæ may be almost constantly poured into it from an ulcerated bowel. It has already been pointed out in a previous paper that rational treatment has brought about a great relative decrease in the frequency of liver abscess as a complication of the intestinal infection.

The way in which amœbæ and bacteria reach the liver, and the manner of abscess formation have been a source of much discussion and are still in doubt. In the case of multiple abscesses, the evidence is fairly conclusive that the portal circulation acts as the means of transmission of the infection and indeed, no other explanation is at all satisfactory. No doubt this is also the principal channel by which the amœbæ are transferred when a single abscess manifests itself, but there are also valid reasons for believing that the latter are sometimes formed by the amœbæ following directly continuous tissue. This view is strongly upheld by a number of careful observers who maintain that amœbæ may even at times wander across the abdominal cavity and attack the liver at the apex of the dome. The rather frequent occurrence of subdiaphragmatic abscesses in places where the liver is not covered by its capsule is used as an argument in favor of this hypothesis. I have seen a few intestines in which the extensive ulcerations and adhesions about the hepatic flexure were so clearly associated with the abscess as to suggest direct infection. Other examples showing the disposition to wander which the organisms possess, are seen in the occasional amœbic pulmonary abscesses and empyemata which occur without liver abscess or other abdominal lesions. However, even after all these rarer occurrences have been taken into account there still remains the great majority of abscesses the presence of which can only satisfactorily be explained by assuming the portal venous system to be the channel of transmission, and, when we consider the histologic findings which are derived from a study of the intestinal infection, it is surprising that liver abscesses are not more frequent. Amœbæ, at times in great numbers, may frequently be seen in the blood vessels contiguous to the intestinal ulcers; in fact, where the lesions are extensive this may constantly be observed. These organisms may also be found in blood vessels in the intermuscular septa

and in other situations at considerable distances from the macroscopic lesions. In addition, amœbæ have been reported as occurring in emboli in the portal veins, and since this fact was first pointed out by Councilman and Lafleur and other observers, I have found it to be true in two instances, and in neither of these was there abscess or other indication of gross amœbic infection of the liver. Therefore, the evidence seems to be conclusive that in the majority of cases of well-advanced intestinal infection, amœbæ must almost constantly be carried to the liver, and this is particularly true in respect to those in which the thrombosis and endarteritis are modified by secondary invaders. If this is so, then actual liver infection must, at least partially, depend upon changes in that organ itself. However, in accepting such a tentative conclusion, a few other considerations must be advanced. The first and most important of these, namely, the influence of environment or symbiosis on the pathogenic action of amœbæ, has already briefly been dealt with by Musgrave and Clegg.[4] From this work and since that communication, from experimental data which we have obtained with cultures of amœbæ, it seems fairly established that these organisms are amenable to changes of environment which at first they would not easily tolerate. When such a change has been made, they are brought back to the original symbiosis with an equal amount of difficulty. The power of an amœba to propogate under new conditions may, to a large extent, depend upon the similarity between its new environment and the former one and also possibly, although this has not been proved, upon its ability to produce lesions in the tissues. If this should be true of intestinal infections it might be equally so of those of the liver, and the occurrence of liver abscess would then depend, as it apparently does, not so much upon whether amœbæ reach the liver or not, but upon whether or not the liver environment had, by both previous and present sub-intoxication, caused by the intestinal environment (see Adami's articles), been brought to a condition approaching that of the bowel in which the amœbæ were acting. This question is an extremely important one because in its answer by the use of cultures lies the possibility of an explanation of the exact mode of action of amœbæ in producing pathologic lesions. For work of this class the liver is a much more suitable organ than the intestine, because of the large variety of bacteria and other unknown influences in the latter. At present all of my work being carried on in conjunction with M. T. Clegg, of this laboratory, and in St. Paul's Hospital is in the direction indicated above, but the results so far obtained do not justify further statements.

Mouton, working with cultures of amœbæ, opened up another approach to this subject by studying the action of various serums upon "amœba diastase."

[4] *Publications Biological Laboratory, Bureau of Government Laboratories*, Manila (1904), **18**, 1.

The specific cause of this type of liver abscess is *Amœba coli,* either acting alone or in association with certain other micro-organisms. These parasites are constantly present in the contents or walls of true amœbic abscesses and no apparent differences are found between the amœbæ encountered here and those seen in the intestine. They may be the only organisms to be observed in the abscess at any time, or both amœbæ and bacteria may be present throughout the course of its growth, or, again, bacteria may be associated with amœbæ in the early lesions only to disappear at a later period. Both amœbæ and bacteria are often in the end not found in the contents of abscesses in which they were present at the beginning. Frequently the bacteria produce alterations, particularly in the nature of the lesion, so that it ultimately may more closely resemble a bacterial abscess. The bacteria which are encountered are of several different varieties. *S. pyogenes aureus* and *B. coli* are the most frequent; streptococci, pneumococci, *B. pyocyaneus* and several others have occasionally been found.

Bacteria are much more commonly associated with amœbæ in multiple abscesses than they are in solitary ones. This fact has been pointed out by Rogers and others and these observations are confirmed by the findings in the Philippine Islands. Multiple abscesses, sterile according to culture and animal inoculation, are occasionally met with, but this occurrence is much less frequent than it is in the large, solitary ones. In considering the reasons for this condition, several circumstances must be taken into consideration. Multiple abscesses are usually smaller and of shorter duration than are the single ones, and it is probable that, were opportunity offered at an early stage for bacteriologic study of solitary abscesses, more of them would show bacteria. In fact, to judge from the behavior of amœbæ on artificial media, it would hardly seem as if these organisms would be able to reach the liver, free from bacteria. No doubt, multiple abscesses are usually transmitted through the portal vessels, and under these circumstances bacteria within and attached to the amœbæ have a better opportunity of living and of multiplying than they would in some of the cases in which they probably reach the liver by directly continuous tissue.

A determination of the time of development of liver abscesses with reference to the bowel infection is not possible in the majority of instances. This is largely due to the slow development and absence of early symptoms in both diseases, however, the evidence tends to show that abscess may develop at any time during the intestinal infection. The literature on liver abscess in dysentery contains references to abscesses which have developed from a few days' time after the onset of the dysentery to those in which the affection was first diagnosed twenty-one years after the beginning. These records are based upon clinical evidences as given by the diagnosis of both the disease of the colon and of the liver, and therefore they are absolutely valueless in determining the only

question worth considering, namely, the shortest and the usual time elapsing between the development of the intestinal infection and the formation of the abscess. It has already been shown in previous papers that the appearance of diarrhœa and of other dysenteric symptoms bears little relation to the actual duration of the intestinal disease, and similar conclusions are true of the liver infection. The course of the disease, as will presently be shown, is slow and the diagnosis of uncomplicated abscesses is not usually possible at an early period.

The course and termination of amœbic liver abscess are both most certainly influenced by the bacteria which may be present therein. Multiple abscesses showing combined amœbic and bacterial infection, develop quite rapidly, and they usually terminate without perforation in the death of the patient, with a septic temperature. The same type when it is of purely amœbic etiology, has a slower course, the toxæmia is not so great, and patients often die of intercurrent trouble, with or without perforation of the abscess. In large single abscesses the course is still more chronic than in the latter case, and here also bacterial infection influences the variation and the outcome. It is undoubtedly true that, at times, patients having large, single amœbic abscesses of the liver remain in fair general health for several years.

Amœbic abscesses in general terminate in several ways. Where bacteria are associated with amœbæ, death may result from sepsis. A general amyloid condition is sometimes encountered at autopsy, as a result of the chronic sub-intoxication often seen as a sequel of large abscesses. Single ones are sometimes arrested and encapsulated, and may only be discovered at autopsy, years afterwards, or again they may completely heal. However, perforation is the most common termination, particularly of single abscesses, or of cases in which there are only a few large ones present and this may take place either externally or into any of the contiguous structures. By far the most frequent perforations are into the right lung or pleural cavity or into both. However, empyema of the left side, or pulmonitis may also occur, and this must be borne in mind as a possible favorable termination of abscess in the left lobe of the liver. The diagnosis of abscess in this location is much more difficult than when it occurs in other situations and surgical intervention is less likely; therefore, a larger percentage of these abscesses ruptures than of those of the right lobe. Perforations also occur into the abdominal cavity, intestine, stomach, vena cava, pericardium, retroperitoneal tissues, psoas muscle, kidney, urinary bladder, gall bladder, or spleen. I saw one case in the Army and Navy Hospital, Hot Springs, Arkansas, with perforation into the right pleural cavity, right lung, and externally through the skin. This patient recovered.

Symptoms and diagnosis.—The clinical picture varies greatly. Sometimes a large abscess may develop but slight symptoms and the diagnosis is not always possible even by exploratory puncture; however, in the

majority of instances the clinical findings will justify a diagnosis, which may be confirmed by evacuating a portion of the contents of the abscess through an exploring needle. Experience teaches the physician to be conservative in making these diagnoses during life, because fever, enlargement of the liver, pain, and the other common symptoms and the usual results of blood examinations may be quite well marked without the presence of an abscess, and again, a fairly large abscess may show almost no symptoms, even after a most complete and careful examination.

Physical signs.—The liver usually shows some enlargement, particularly if the right lobe is involved, and Osler has pointed out that this enlargement is usually more upward than it is downward. However, this condition is not so important in the Tropics, where some enlargement of the liver in foreigners and others most liable to abscesses is of rather frequent occurrence—the so-called "tropical liver." However, not infrequently rather extensive liver abscesses are found post-mortem, without any appreciable enlargement of the organ.

Fever—remittent, intermittent, or continuous—is usually present, but sometimes the temperature remains normal throughout the course of the disease. Septic temperatures are probably always due to mixed infections of amœbæ and bacteria in the abscesses. Two cases without fever at autopsy revealed solitary sterile abscesses of the right lobe. The fever is not at all characteristic. Not only may it be of any type, or on the other hand entirely absent, but the exclusion of other etiologic agents to which its production may be due is not always practicable. I desire to call particular attention to the fever which may also be caused by non-suppurative trouble of the liver. This is often present, and with local inflammatory conditions and adhesions about the hepatic flexure it makes a very deceptive picture. Rigors and sweats are usual with septic cases.

The blood count.—The number of the leucocytes and, particularly, their differential count, is generally given an undue importance in the symptomatology of this disease in the Tropics. Neither of these are of very great value in diagnosis. The intestinal infection is often responsible for a leucocytosis, which, when the associated bacterial infection is such as to give rise to acute dysenteric symptoms, may even reach above 20,000 for days or weeks at a time. Sometimes, with but slight intestinal symptoms, a moderate leucocytosis may be due to localized inflammation about the hepatic or splenic flexures or the cæcum. Frequently, all the suspicious symptoms of liver abscess, including the leucocytosis, disappear permanently after a few saline purges and large quinine enemas.

The *pain* of amœbic abscess is rarely acute and is not so frequently referred to the shoulder as it is in other kinds of abscess or in that of mixed infection. In the solitary, sterile abscess the pain is more of the nature of a general soreness over the liver and tenderness is usually found on pressure over its lower border or over the gall bladder. When the

abscess is of the sub-diaphragmatic type, pain is usually increased by a change of position, particularly by lying on the left side or by standing. In one case this dull, sore pain on standing or lying on the left side was the only subjective symptom of a subdiaphragmatic abscess; and this symptom disappeared before the diagnosis was made as a result of the perforation by the abscess into the lung. The local pains are most pronounced in superficial abscesses accompanied by perihepatitis, and the radiating ones in deeper disturbances and in septic conditions. As has already been mentioned, intestinal infection with inflammation and adhesions about the upper flexure of the colon may, in these instances, be deceptive.

The respiratory system.—Where abscesses rupture into the lung or pleura disturbances occur in the respiratory system. This is also the case when there is inflammation between the liver and diaphragm, or between the diaphragmatic and parietal pleuræ, a condition which sometimes occurs without actual extension of the liver abscess into the chest. No difficulty will be found in diagnosing an amœbic empyema. The lung is frequently the seat of lesions caused by rupture of the liver abscess and the diagnosis can be made by finding the parasites in the sputum.

Jaundice of a marked type is rare in solitary abscesses, and not very frequent in multiple ones. A slight subichteric tinge is quite common, but this is equally so in the non-suppurative hepatitis often associated with intestinal diseases. Except in septic conditions, there are no *stomach* symptoms of importance. There may or may not be nausea and there rarely is vomiting. One very important point which has not been properly emphasized is the influence which liver abscesses frequently exert on the intestinal symptoms. An increase in the number of the bowel movements during the development of abscesses is, to say the least, sufficiently common to be suggestive, and the removal of the liver pus by operation is nearly always followed by a temporary improvement in the number and character of the bowel movements.

Summary.—The symptoms of amœbic liver abscess vary greatly and may entirely be absent for long periods of time—sometimes for years. The diagnosis of the disease depends more upon the general picture, after excluding other diseases, than upon any system of direct examination. In the Tropics, the symptoms of an amœbic liver abscess may largely be the result of other conditions and diseases present at the time, and therefore these symptoms sometimes exist without liver abscess. In all cases the diagnosis should be confirmed by exploratory puncture and it must not be forgotten that even by this means a large abscess may not be located after very persistent use of the exploring needle. The diagnosis during life or before perforation is sometimes impossible and this is particularly true when the abscess is situated in the smaller lobes of the liver and in other inaccessible places. Except to differentiate between a situation in the right or left lobe, exactly to locate the abscess is

rarely possible, although this may occasionally be done by close, persistent observation and study.

The prognosis in multiple, inoperable, and septic abscesses is bad. In the solitary abscess which can be located, it is very good when the patient is in the hands of a competent surgeon. The treatment is surgical.

Abscess formations in locations other than the liver are occasionally seen. They most commonly result from perforation and may occur anywhere in the region of the colon, from the rectum to the cæcum. Perhaps the most common location is near the cæcum where, if abscess can be diagnosed, operation offers good chances of recovery. These lesions vary greatly in size and often in their development involve important structures such as the peri-renal tissues, the psoas muscle, the appendix, the abdominal wall, and sometimes the kidney itself. Large, ischio-rectal abscesses may occasionally result from a perforation in the rectum and in one such case, which will be discussed below, a large quantity of amœbic pus was evacuated. Abcesses occurring along the descending colon may be of a dissecting type and cases may be seen at necropsy, where, owing to perforations, adhesions, and ulceration, the entire intestinal wall may have sloughed away leaving a continent channel partly formed by the abdominal wall and adjacent structures. In rare instances, small abscesses formed and held in place by adherent omentum may be encountered on the anterior surfaces of the colon. One found in the descending colon at autopsy contained about 20 cubic centimeters of pus. Abscesses have also been reported in the parotid gland, the floor of the mouth, the brain, etc.

Gastro-intestinal complications are very frequent and the after effects of dysentery on the upper portion of the alimentary tract are still more important. However, in the Tropics, a variety of disorders and diseases of this system are so frequently met with that it is very difficult to determine just how specific the relation to amœbic infection is and just which of the various troubles are most dependent upon this specific parasitic infection. Amœbæ are rarely found in the alimentary tube above the ileo-cæcal valve, and it is probable that the majority of diseases encountered in this portion of the bowel are not in a direct way dependent upon the amœbæ, but rather upon the associated dusturbing factors which so frequently attack the colon itself. In other words, the amœbic infection is usually a compound one and some of the symptoms in the colon and the majority of those above that portion of the bowel are due to agents other than the amœbæ. Most of the gastro-intestinal complications of amœbiasis develop rather late in the disease and may more properly be considered as sequelæ, or after effects, but some should also be mentioned here.

Cancrum oris has frequently been pointed out as a complication in dysentery and it is occasionally seen in the amœbic variety; however, it is perhaps met with less frequently than in the catarrhal, Shiga, or

streptococci types. It is of course most often observed in the terminal dysenteries occurring in the course of Bright's disease, diabetes, etc. Formerly this complication was seen more often in the Philippine Islands. Its disappearance has been due largely to the better care and treatment it is possible to give patients now than it was formerly. It is not clear or probable that *Cancrum oris* is directly associated with a specific infectious colitis in any form; it appears rather to be more dependent upon constitutional conditions.

Stomatitis and esophagitis occur more frequently as after effects of the disease, but sometimes do exist during its earlier stages. Superficial ulceration of the mucosa is the usual type of both these conditions and they are apparently always associated with lesions in the stomach and small bowel. Clinically, these are very important complications because they often are present before the gastritis and enteritis are marked enough to indicate the general condition of the tract. The appearance of the stomatitis is always a signal for more careful treatment, or the general condition of sprue will be the sequel.

Stomach disorders are particularly frequent in Manila and naturally are often associated with amœbic disease in a casual manner. However, in addition to this, there is more frequent and undoubtedly mutually dependent association between the two conditions, particularly in the later stages of a prolonged amœbic infection. The stomach symptoms which most interest us here are those of gastritis, gastralgia, and gastric ulcer. Gastralgia is particularly frequent and may be present with but a mild amœbic infection. The different types of gastritis with achylia gastrica and hyperchlorhydria are seen and gastric ulcer is relatively more frequent than in other diseases. All these conditions, together with nausea and indigestion, are undoubtedly made worse by rectal irrigations. In gastric ulcer it may occasionally be necessary, if indeed not always wise, to suspend large colon irrigations. In two cases of this combination recently studied in St. Paul's Hospital, gastric hemorrhages ceased with suspension of the colon irrigation which was being employed in the treatment of the dysentery. Hyperchlorhydria is, as a rule, also much aggravated by colon lavage.

Enteritis occurs with about the same regularity and in the same class of patients as does gastritis. In addition to the stomach troubles, it is one of the most important complications of the disease because of the ultimate results due to lack of assimilation of food. Reversed peristalsis from local treatment of the dysentery is not uncommon and often very annoying.

Renal complications, and particularly hæmorrhoids, are frequent, while fissures and fistulas occur less often. Hæmorrhoids are usually aggravated by treatment, and in some instances seem to owe their origin to it.

Complications of the large bowel are perhaps the most interesting and frequent, and the least written about. Particularly may be mentioned

dilations, contractions, and cicatricial formations of the bowel; other types of infection and of dysentery, such as the specific bacterial, gangrenous, diphtheritic, catarrhal, and miscellaneous types; and those terminal ones to be seen in nephritis and other constitutional diseases.

Dilation of parts of the colon are frequently encountered and almost general dilation is occasionally observed post-mortem. The latter condition may also be diagnosed during life. Whether they are either general or local, dilations are made possible by the relaxation of the circular and longitudinal muscular bands of the intestine. In advanced cases the bowel takes on the appearance of a smooth tube with partial or complete absence of the rugæ and folds. The picture is rather that of a post-dysenteric process than that of a complication during the active stages of the disease. However, it is also seen as a complication at times. One patient who died recently in St. Paul's Hospital showed this condition in a marked degree. The amœbic disease was probably of several years' duration, and death was due to an acute streptococcal dysentery lasting only a few days. At autopsy, the width of the opened bowel measured on an average 15 centimeters, and in the cæcum it reached 20 centimeters. The clinical manifestations of such dilation are interesting. When it occurs early in the disease it is usually, if not always, associated with troublesome gas collections in the bowel and a tendency to constipation, but as an after effect, the sprue diarrhœa is its constant associate. Deep, undermined ulceration is rarely found in an intestine of this nature and it does not appear, as might be supposed, that intestinal irrigation has to do with its production.

Cicatricial contraction from healed amœbic ulcerations is observed less frequently in the Philippine Islands than it is stated to be in other parts of the world. It is occasionally seen in a moderate degree, and sometimes to such an extent as to cripple the bowel function, but on the whole it is of but little importance as a complication in this country.

Other dysenteries and bowel diseases complicate amœbiasis with great frequency and have not received the careful study which their importance merits. The acute bacterial dysentery (Shiga) has not been very frequently encountered in the Philippine Islands for some years, but there have been undoubted cases where it has complicated the amœbic infection and others where it has preceded or followed such disease. The combination is an exceedingly difficult one to treat; the pathologic picture is modified and the diagnosis difficult on account of the tedious methods necessary for the isolation of *B. dysenteriæ* from the stools. The serum reaction is not of very great clinical value. The bacteriology of all of the acute dysenteries is not known, but there surely are organisms, in addition to Shiga's bacillus, which under proper conditions play an important etiological role. It is also likely that this group is greater in the Tropics than in the temperate zones, and also possible in these regions that there is an increased virulence of some of the well-known

organisms, perhaps caused by their changed environment, and also a decreased resistance on the part of the patient. The possibility of the influence of symbiosis with animal parasites on the virulence of such organisms as the colon bacillus needs to be elucidated. Whatever the etiologic factors may be, it is a fact that the engrafting of acute dysentery on an old amœbic process is of quite frequent occurrence in the Philippine Islands. The character of the amœbic lesion is too far removed from those seen in such conditions as to admit of any other interpretation than a double etiology. Diphtheritis, gangrene, folliculitis, etc., are common complications and bear little or no relation to amœbic etiology. The ulcerations in the terminal dysenteries in nephritis, diabetes, splenomegalies, cirrhosis of the liver, and other diseases may, as pointed out in previous publications, complicate amœbiasis and alter the clinical picture, pathology, and prognosis very materially.

Finally, there remains to be mentioned here the association of intestinal parasites, such as paramæcia, strongyloides, oxyuris, trichomonas, circomonas, megastoma, tænia, trichuris, ascaris, and others with amœbæ. Some of these parasites, particularly *Balantidium coli* and *Strongyloides intestinalis,* are now quite generally acknowledged to be pathogenic parasites, but many others are likewise considered to be harmless. However, I believe the almost unanimous concensus of opinion of the careful, experienced workers in Manila is voiced in the statement that some of these so-called harmless parasites are disease producers. For example, many men here recognize a diarrhœa caused by monads. Several types of these parasites, when present in large numbers, are very intimately connected with chronic diarrhœa and they are surely much more important than they are generally considered to be.

Megostoma entericum (*Lamblia intestinalis*) deserves particular notice. It is often found and, when encountered in great numbers, it is *always* associated with chronic diarrhœa, which disappears with the destruction of the parasites. In my opinion, this flagellate bears a decided causative relation to the diarrhœa. Even the *Trichuris trichuria* certainly produces small, hæmorrhagic spots where it adheres to the mucosa of the cæcum and some of these, as in a case now being studied, are closely associated with very early amœbic lesions. Whatever pathological significance may be attached to these parasites in general, some of them, particularly the actively motile ones, such as monads, surely aggravate amœbic ulcers in which they may be present.

Perforation of intestinal ulcers is one of the very frequent complications of untreated and of fatal cases, but is comparatively rare when proper therapy has been instituted early and followed persistently. These perforations may occur in various places and give rise to acute general peritonitis, localized peritonitis, or abscess formations.

Strangulation of either the large or small intestine may occur from several causes. Partial or complete strangulation from external pressure

by fibrous bands following localized peritonitis deserves special attention because it is not so infrequent and because it has previously received but slight consideration. Rogers mentions a case of strangulation of the small intestine from such a cause, and I have observed several cases, post-mortem, in which such bands were placed in a manner in which they must materially have interfered with the function of the organ. These conditions may exist in any portion of the colon, but they are most common below the splenic flexure; one case has been encountered where an hourglass contraction of the cæcum was due to such a cause. The omentum is a factor in the majority of these cases because it is the important agent in the localized peritonitis which is very frequent in the disease. Many of the fibrous bands are formed principally about the omental-intestinal adhesions. Except in very rare instances, these contractions do not produce results which contribute materially toward a fatal termination of the disease, but, on the other hand, they are the cause of certain symptoms, both during the course of the disease and afterwards, in patients who recover. The symptoms usually are not of such a nature as to allow of a definite diagnosis of the condition, nor are they of very great importance, excepting where some other condition is to be excluded.

Intestinal hæmorrhage is a comparatively rare complication of amœbic infection, as is to be expected from the histologic picture which is produced, such as the well-known thrombosed condition of the blood vessels within and closely surrounding the lesions, and the more or less well-marked endarteritis which is usually present. Hæmorrhage has been noted in a general way by several writers, but its importance as a factor to be reckoned with in the prognosis and treatment of the disease has not, until recently, received very much consideration. Attention had been called to it, in dysentery, by Woodward, Scheube, Manson, Sodre, Osler, Lafleur, Ranaud, and others, but its special importance in relation to amœbic dysentery has been emphasized by Lafleur, Haasler and Strong. The association of these hæmorrhages with liver abscess has also been noted by Woodward, Haasler, Strong, and Mugliston and Freer.

Haasler [5] briefly reported three cases of severe intestinal hæmorrhage in amœbic dysentery, in two of which the hæmorrhage was considered to be the cause of death. The author notes particularly that in both of these cases there was liver abscess and in one, with death after a loss of over 4 liters of blood, a thrombosed vessel was found in one of the ulcers. Strong [6] again emphasized the occurrence of severe intestinal hæmorrhage as a fatal complication of amœbic dysentery, and reported to the Manila Medical Society November 2, 1902, two cases of amœbic dysentery and liver abscess in which severe hæmorrhage was the cause of death. One of the patients lost more than 2 liters of blood in repeated hæmorrhages during the three days preceding the end. At necropsy the source of hæmorrhage was

[5] Haasler: *Deutsche Medicin. Wochenschr.* (1902), **28**, 26 and 47.

[6] Strong: *Publications Biological Laboratory, Bureau of Government Laboratories* (1905), **32**, 1.

found in a thrombosed vessel occurring in an ulcer situated about 5 centimeters below the cæcum. In his other case the point of hæmorrhage was not located at autopsy. He also later reported two more similar cases, again emphasizing the presence of liver abscess. In one of these he called attention to the delayed coagulation time of the blood.

Mugliston and Freer[7] report two cases of amœbiasis with abscess of the liver and fatal intestinal hæmorrhage. Both of these had septic temperatures and in one, jaundice during life was noted.

I have seen one fatal and four other cases of severe intestinal hæmorrhage in amœbiasis without liver abscess. In the fatal case, a native prisoner, the amœbiasis was associated with Banti's disease and the hæmorrhage was both gastric and intestinal. One patient, with two hæmorrhages aggregating about 1,200 cubic centimeters of blood in twenty-four hours, also had an amœbic, ischio-rectal abscess. In one, with repeated small hæmorrhages, there was also tuberculosis of the bowel and in the remaining two there was some severe secondary invader in the intestine, as was shown by the severity of the symptoms, which included fever, tenesmus and depression, conditions which probably do not occur in uncomplicated amœbic infections.

Strong discusses the relations between liver abscess and severe fatal hæmorrhages and refers first, to the question of whether the destruction of such large amounts of liver tissue may not sometimes bring about serious functional disturbances in this organ and lead to a condition which predisposes to hæmorrhage; second, to the mechanical interference caused to the portal circulation; third, to the relation between hæmorrhage and various other diseases of the liver, particularly when jaundice is present; fourth, to the diminished coagulability of the blood; and fifth, to special bacterial (toxic) activity. He also suggests the occasional possible diagnostic importance of such hæmorrhages in liver abscesses.

I am of the opinion that the association between amœbic liver abscess and hæmorrhage is because of an interdependence upon a common condition which is discussed more fully under abscess of the liver. It will be noted, in looking over the literature of intestinal hæmorrhage in dysentery, where the records are specific there is often evidence of severe infection which can not be attributed to amœbæ, and this is particularly true in the cases associated with liver abscess. Strong's and Mugliston's and Freer's cases had slight jaundice; there was fever and other evidences not found in amœbic infection without the presence of some other etiologic agent and which, by their action, might bring about the general conditions which favor intestinal hæmorrhage in other diseases. In discussing the etiology of these hæmorrhages we must not lose sight of the condition of the intestine, particularly with reference to the nature of the secondary invaders which may be present. The majority of the cases which have been reported were in infections of a gangrenous or

[7] Mugliston and Freer: *Jour. Trop. Med.* (1905), **8**, 113.

diphtheritic or other very severe type, the lesions in which were clearly not due to the action of the amœbæ. We know that such agents may alter the whole type of an amœbic lesion and bring it histologically nearer those in which bleeding is a more common occurrence.

The symptomatology and treatment of intestinal hæmorrhage caused by amœbic ulceration is the same as when it is due to other causes and need not be entered into here.

Sloughing of the mucosa is preëminently a complication of this disease and in untreated cases is fairly frequent. The sloughs may be of any size, from small shreds to casts of the bowel several centimeters in length. Sometimes at autopsy, considerable areas are seen completely denuded of mucosa.

Amœbic appendicitis.—Involvement of the appendix in amœbic infection of the colon has been noted by several writers. It has already become a subject of considerable importance in the Philippine Islands, and the larger number of patients returning to the United States from Manila and other tropical countries makes it of considerable importance to the profession at home. In my first report [8] of 150 post-mortem examinations of fatal cases of intestinal amœbiasis, 100 of which were from the records of Strong and myself, 6 per cent showed amœbic lesions in the appendix and in 7 per cent more there were other lesions of this organ and 1 case had amœbic ulceration engrafted on an old, chronic appendicitis of other etiology. In a second series of 100 fatal cases reported by Woolley and Musgrave [8] there were 8 with amœbic lesions in the appendix and in all, as in the first series, the lesions appeared as a continuation of an amœbic process in the cæcum; in the last series they also appeared in the small intestine, just above the ileo-cæcal valve. The above and many additional pathological data which have been obtained, together with a large amount of clinical material, is the basis for the present consideration of the subject.

Etiology.—The disease is much less frequently met with at autopsy than one would suppose, judging from clinical observation. It was formerly more common than it is now in the Philippine Islands. This decrease is largely due to the more general early diagnosis and successful treatment of the colon infection at the present time. It is nearly or quite always an extension of the amœbic process from the cæcum and shows a specially marked relation to infection on and above the Bauhinian valve. It probably does not often develop early in the disease, for it was not present in a single one of 25 early cases reported by Woolley and myself,[8] in which death was caused by intercurrent diseases. It most often attacks an otherwise normal appendix and but rarely one already crippled by former disease, and it is very much more frequent in severe dysenteric infection, with intercurrent diphtheritis, gangrene, etc.

[8] *Loc. cit.*

Morbid anatomy.—The lesions of the amœbic process in the appendix resemble those found in the bowel, but they are usually smaller and more superficial. Microscopically, the same general picture including thrombosis of the vessels, is seen. As in the colon, the ulcers are rarely along the meso-border but they sometimes may extend entirely around the mucosa. The appendix is most often patulous, with a rather large lumen, and concretions are exceptional. External evidences of inflammation are not very marked; as a rule, they consist of moderate engorgement and injection of the vessels.

Symptoms and diagnosis.—There is not very much to add to the general symptomatology as given in a previous communication.[9] The clinical manifestations in general resemble those in appendicitis from other causes, but are as a rule less severe. There is less rigidity of the abdominal muscles, the tumor mass is not so sharply circumscribed, and the fever and general prostration are less marked. However, cases may be of a fulminating type and are then not to be distinguished clinically from other types of appendicitis, but then these, like very acute intestinal symptoms, are due more to secondary invaders than to the amœbic infection. Appendicitis, in no way caused by amœbæ, may occur in a patient suffering from amœbic dysentery. The leucocyte count is not of as much value in amœbic appendicitis as it is in other types, because the intestinal infection plays too uncertain a part in the variation of the number of the white cells. The following pathologic changes found in intestinal amœbiasis may give clinical symptoms closely resembling appendicitis and must be taken into account in a consideration of the subject:

(1) Severe amœbic infection of the colon or cæcum and ascending colon.

(2) Infection of the lower ileum with the cæcum.

(3) Acute, localized peritonitis about the cæcum, ascending colon, or hepatic flexure.

(4) Pericæcal amœbic abscesses.

(5) Neuralgia, gaseous distention, and fæcal accumulation in the cæcum.

(6) Acute catarrhal appendicitis.

(7) Chronic recurrent appendicitis.

(8) Chronic recurrent appendicitis with secondary amœbic infection.

(9) Amœbic appendicitis.

(10) Any combination of the above conditions.

The first of these conditions is a *very* frequent one in Manila and superficially at least, it closely resembles appendicitis. The differentiation, however, is not, as a rule, difficult upon careful clinical examination by one familiar with all the conditions. The fever, leucocyte count, nausea, and

[9] *Loc. cit.*

vomiting (particularly if the patient is taking enemas), abdominal tenderness, etc., may indicate appendicial involvement, but the history of the case, careful palpation and percussion, lessened or absent rigidity of the abdominal muscles, the area and diffuseness of the tenderness and the location and character of the tumor mass, make the diagnosis fairly easy in the majority of instances. This is the class of cases where frequent and needless appendicectomies are done by some physicians with more surgical ambition than judgment. Having performed the autopsies on a few of these, examined the removed appendices in several, and later treated the condition of the bowel in a number of others, I can not condemn this practice too severely. The operation in this class of cases is not only useless but dangerous, because of the delay which it causes in the treatment of the condition of the bowel.

Cases which may be classified under the second, third, and fourth headings very closely resemble, in clinical symptoms, the class just described and two or more of the conditions are, in fact, often combined. It is not possible to diagnose amœbic disease of the lower ileum with certainty. Acute, localized peritonitis and other adhesions about the cæcum frequently occur, particularly in severe infections and are usually quite painful. The omentum is often plastered about the cæcum and adjacent structures and, when the bowel is empty and there is not too much tenderness, the condition should be recognized by the experienced examiner. Pericæcal amœbic abscesses are usually recognized by the same manifestations as are those from other causes; they have a strong tendency to spread into the surrounding tissues.

Gaseous distention and even fæcal accumulations in the cæcum are frequently met with in patients taking enemas and often give rise to a painful condition. The symptoms may be relieved by an active cathartic, which should also be used before a final diagnosis of other conditions in the region of the cæcum is attempted. Severe symptoms are often permanently relieved by one or two doses of salts.

Acute, catarrhal appendicitis may, of course, occur during the time a patient is suffering from intestinal amœbiasis. This complication, curiously enough, is comparatively rare, but when it is the case the symptomatology and treatment are the same as in appendicitis occurring in an otherwise healthy person.

Chronic recurrent appendicitis is no more or no less frequent in this disease than in other classes of patients. Recurrences in appendices where amœbic infection is present are sometimes due to close association with the diseased cæcum. An amœbic infection is sometimes engrafted upon such an appendix, but this is of very rare occurrence and the diagnosis is then not only difficult but often impossible.

Primary appendicitis is the most frequent type of amœbic infection of the appendix. Its clinical manifestations, when there is an occlusion, closely resemble acute appendicitis from other causes. These infections

are almost always accompanied by an extension of a severe diphtheritis or other secondary involvement of the cæcum. There are a number of cases of a very mild type of undoubted amœbic ulceration of the appendix, accompanied by the discharge of material through the patent lumen, with recovery under medical treatment. Unless there is some severe secondary invader, the amœbic lesions are particularly apt to be near the cæcum, and, when more distant, are less likely to produce serious trouble than in any other type of appendicitis. All varieties of combinations of the ten headings given may be encountered, and to deal successfully with them requires a close study of the individual cases and a comprehensive knowledge of the subject.

Prognosis and treatment.—If proper treatment is given, the prognosis is usually good in nearly all the conditions mentioned above, and it is particularly so when the appendix itself is not actually involved in an acute catarrhal or amœbic infection. However, in quite a number of patients when the symptoms which have been detailed supervene in a case complicated by very severe diphtheritic or gangrenous cæcum or appendix, the outlook is bad, regardless of the treatment. The treatment of most of these conditions is medical, under close surgical consultation. Large, high enemas combined with saline cathartics and local applications permanently relieve most of these patients. When the appendix is really involved, although many of these cases undoubtedly get well under medical measures, the treatment should be surgical, but of a conservative nature. Great care in diagnosis should be used and unnecessary surgical intervention carefully guarded against, because the operation of necessity delays treatment of the dysentery. This may prove a very serious matter and in some instances in Manila has surely been responsible for the fatal outcome. The operation of appendocostomy or cæcostomy, as advocated by Tuttle and others, might occasionally serve a double purpose in these patients. This operation has been performed several times in Dr. McDill's surgical service in St. Paul's Hospital and the cases will be fully reported by him.

Anatomic displacements and malformations, such as ptosis, unusually long mesentery, diverticula, etc., may be of serious enough import to be classed as complications. Enteroptosis, consisting of a V-shaped descent of the transverse colon which consequently forms a sharper angle at the hepatic and splenic flexures of the colon, may become of particular importance, due largely to the proneness which these two points have to severe amœbic involvement and the difficulty of securing satisfactory irrigation of such a bowel. Such positions of the transverse colon are not infrequently seen at autopsy and are to be at least partially, explained either by the increased weight of this portion of the intestine due to inflammation or to adhesions between the intestine and omentum and some portion of the abdominal wall. Unusually long mesenteries and peculiar flexures in the sigmoid and rectum deserve to be mentioned because of their importance in the introduction of rectal tubes.

ACUTE, GENERAL PERITONITIS usually follows perforation of an ulcer in the colon, or of a liver abscess, but this complication does occur without any perforation whatever and, on the other hand, perforations of the ulcers in the colon may be walled off without general peritonitis. In rare instances, the rupture of a liver abscess into the peritoneal cavity may take place without producing general peritonitis. In 100 carefully examined, fatal cases of amœbiasis, acute general peritonitis occurred 26 times; 4 times from ruptured liver abscesses; 20 times from perforation in the large bowel; once from a perforated appendix, and once without any perforation. Of the colon perforations, 8 were in the sigmoid flexure and descending colon; 2 in the transverse colon and 9 in the ascending colon and cæcum. In the case of peritonitis without perforation there was a combination of acute and amœbic dysentery. These statistics are, of course, from extreme cases and in no way represent the prevalence of peritonitis in any other class. It is comparatively a rare occurrence in patients who are satisfactorily treated and even in an average series of fatal cases it will be found much less frequently than it is in the statistics quoted above. The symptomatology and treatment of this complication needs no comment here.

CHRONIC, LOCALIZED ADHESIVE PERITONITIS is one of the most frequent complications of the amœbic infection and is found in more than 80 per cent of the fatal cases. It may be very slight or very extensive and may give rise to all varieties of adhesions which may occur in the abdominal cavity. Some of the most important of these adhesions are of the omentum to the various other adjacent structures, such as to the abdominal wall, the surfaces of the intestines, the appendix, and particularly to the cæcum; of the surfaces of the intestine to each other, to the abdominal wall, the appendix, stomach, gall-bladder, liver, spleen, etc.; and the adhesions between the liver and diaphragm, abdominal wall, colon, and even appendix. Many other varieties and combinations are encountered. The principal symptoms of these various conditions are abdominal pain and soreness. They may be so slight as not to be noticed, and, again, may be overshadowed by pains of other origin during the active stages of the intestinal disease. The most annoying manifestation of these adhesions develop as an after effect in this disease, and these conditions will be further considered when that part of the subject is discussed.

PHLEBITIS, EMBOLI, VENUS THROMBOSIS, AND INFARCTIONS have been reported and infarcts in the liver, spleen, and intestine are sometimes seen. Within the last few days multiple, white infarcts of both kidneys were found at autopsy in a case of intestinal amœbiasis combined with mesenteric and intestinal tuberculosis.

PERNICIOUS ANÆMIA has but rarely been noted as a complication in amœbic disease. I have seen two cases in which the association was intimate and an apparent interdependence continued during the course of the disease. Both were patients who had contracted their maladies in

the Philippine Islands and came under my care in the Army and Navy Hospital at Hot Springs, Arkansas. It was impossible to determine which disease antedated the other, but the clinical evidence of the double infection was conclusive. The particularly interesting feature in both of these cases was the parallelism between the clinical manifestations and the blood changes and the bowel symptoms. Temporary improvement in the dysentery was also closely followed by an improvement in the anæmia.

A CASE OF LEUKÆMIA AND AMŒBIC DYSENTERY.—One may be mentioned in connection with these two instances:

This case, like each of the former two, occurred in a discharged volunteer American soldier who had served in the Spanish-American war in Cuba and in the Philippine Islands, and who came under my observation during my service in the Army and Navy Hospital at Hot Springs, Arkansas. The apparent interdependence of the two diseases in this instance was most striking and was studied and confirmed by the late Major Walter Reed, to whom the patient was referred. The dysentery was undoubtedly contracted in Cuba, and enlargement of the spleen was first noticed about eighteen months later, while the patient was serving in the Philippine Islands. The history of the dysentery was the usual one of alternating diarrhœa and constipation, abdominal soreness, and loss of weight. The enlargement of the spleen was progressive. When he came under observation there was moderate emaciation, great weakness, shortness of breath, and slight jaundice. The dysentery was very active. There were from ten to fifteen stools per day, associated with some blood and mucus, and numerous amœbæ. The spleen was very large, extending to the pelvic brim below and beyond the median line to the right. A blood count showed splenic leukæmia with 460,000 white cells. As was mentioned when the two cases of primary anæmia were discussed, the interdependence in this case between the amœbic and leukæmic diseases was decidedly marked, and improvement or exacerbation of one disease was followed by a like procedure in the other. This same general feature has been noticed recently in the study of *splenomegaly*. There have occurred a number of cases of a combination of amœbiasis with splenomegaly, and the association sometimes seems a close one.

CHRONIC RHEUMATISM, both of the articular and muscular types, is very frequently met with in Manila and in many instances seems to bear a very definite relation to amœbiasis as well as to other severe disturbances of the stomach and bowel. Even where alcohol and other recognized causative factors have been eliminated, we still have a frequent association of the two diseases which is hard to explain without acknowledging some form of interdependence. The rheumatic condition is particularly apt to develop in cases of amœbiasis of long standing, and it often shows clinical intensity corresponding to and varying with the condition of the bowel. In other instances, an old rheumatic condition is rendered much worse by an intercurrent dysentery. The clinical evidence is very strongly in favor of dysentery being in some way responsible for one variety of the symptom complex termed chronic rheumatism.

THE NERVOUS SYSTEM, as in the case of chronic rheumatism, often shows disturbances intimately associated with amœbic dysentery. Allen

Starr and other eminent neurologists have pointed out the close association of certain forms of neuritis and neurosis with disturbances of the gastro-intestinal tract, and to these must be added amœbic infection of the colon. Many old, nervous troubles, particularly *sciatica,* are excited by amœbic dysentery, and, in addition to this, the beginnings of various chronic types of nervous disease may be traced to the date of a previous dysentery.

Acute chorea.—There are in the literature a few references to choreic movements complicating this disease, but, so far, no reference to Sydenham's chorea complicating dysentery of any kind has been found. I have seen two instances in which the association of true chorea and the amœbic infection of the colon was very close. Briefly, these cases are as follows:

CASE I. *Intestinal amœbiasis; rather severe infection; acute chorea; recovery; recurrence of both dysentery and chorea; recovery; typhoid fever without chorea; permanent restoration to health.*

Miss X, American, 23 years of age, in Philippine Islands for eighteen months. No chorea in family and no previous history of choreic movements. No history of rheumatism, heart affection, or other disease or tendency to chorea. No previous illness of any kind. After about two weeks of indigestion with intermittent diarrhœa she was taken suddenly during the early evening with acute abdominal pain and nausea. By next morning the bowel movements showed mucus and blood; there was about 1 degree of fever, and tenesmus and nausea were present; microscopically, the fæces contained numerous amœbæ; there was much blood and mucus, sloughs and shreds of mucosa of the bowel. She was treated during the first forty-eight hours with cleansing enemas, mild saline laxatives, and the pain controlled by Dover's powders. On the third day acute symptoms had so much subsided that she was placed on quinine enemas twice daily. The fourth and fifth days were comfortable, no fever, no nausea, but still considerable abdominal pain and rather frequent bowel movements. On the morning of the sixth day choreic movements of the hands were noticed, and by the next the movements were general, including those of the face and legs. There was decided hesitancy in speech; on the tenth day pain and slight swelling of both ankles developed, continued for about twenty days, and gradually disappeared. There was, for some days, considerable tachycardia, the pulse counting from 90 to 105 per minute. The rhythm was a little irregular and a soft, systolic murmur was heard at the apex. There was no evidence of enlargement of the heart, and the murmur disappeared during convalescence. I do not believe there were organic changes in the heart. The chorea and dysentery subsided together during the next three weeks. About six weeks after the onset of the dysentery there was a moderate recurrence of this symptom, although treatment had been continued during this time. With the recurrence of the dysentery, there was return of slight choreic symptoms, confined to the hands and face, and lasting only a few days. Recovery from both the amœbic infection and chorea was permanent. About six months later this patient passed through an attack of typhoid fever. No chorea was seen during this illness, and she has been entirely free from it up to the present time, two years since the dysentery.

CASE II. *Neurotic young woman, 22 years of age. Chorea in childhood, with rheumatism following scarlet fever. Amœbiasis, severe. Chorea; recovery.*

The interesting factors of this case were the relation of the attacks of dysentery to those of the chorea which developed together. The chorea subsided about ten days after the bowel movements had become normal.

In both of these cases the intimate relationship between the dysentery and the chorea was such as strongly to indicate that something was being absorbed from the diseased bowel which caused or aggravated the chorea. When we remember the close association of chorea and rheumatism, and, as just mentioned, that there is also a rather close relation between dysentery and certain cases of rheumatism, the instances described above appear in a more natural light. In both the cases treatment was directed to a cure of the dysentery. In the first one the enemas were stopped for a few days, as it was thought they might have something to do with the trouble, but their interruption was without influence on the character or intensity of the nervous disease.

ALBUMINURIA is very common in long-standing cases of amœbiasis, and organic changes undoubtedly frequently exist as late complications and after effects. However, excepting the association of the two diseases (which has already been discussed) where the kidney trouble is clearly of other etiology, *permanent* impairment of the kidney function does not appear to be a serious outcome of the amœbic disease.

Among the other complications of amœbiasis, which have from time to time been reported, are mentioned fibroid degeneration of the heart, terminal pericarditis, purpura, gangrenous ulcers of the stomach, mastoid abscess, abscess of the brain (Kartulis), pseudoparalysis, gangrene of the foot, etc.

IV.

AFTER EFFECTS.

The degree of restoration of function which will occur after the most extensive amœbic ulceration of the colon has been repeatedly pointed out. In the majority of well-treated cases of simple amœbic colitis there are no serious sequelæ, and even in some of long standing, with the passage of blood and mucus and even of sloughs, regeneration may be so satisfactory that perfect function of the bowel may be restored. However, sequelæ are not rare in amœbiasis, and, while not of so great a variety as the complications, are nevertheless of great importance. Like the complications, they divide themselves into sequelæ directly due to the amœbic infection, those due to the complications of the disease, and those but remotely connected with the amœbic disease. This latter group is a somewhat large one, including constitutional disturbances (conditions arising as a result of wasting, lowered resistance, etc.), and it need not here be entered into in detail. There are several important conditions of the other two groups to be discussed of which the first and one of the most frequent is sprue.

Sprue.—The superficial, clinical picture and the anatomic findings in sprue are fairly constant; enough so, perhaps, to justify its consideration as an entity, but the etiology is surely multiple, *and therefore, at least etiologically, it must be regarded as a symptom complex and not as*

a distinct disease. I have already called attention to this fact in previous publications, and several additional years' experience have confirmed the first observations. This condition is fairly common in the Philippine Islands and is becoming more so as the years go by and we follow our old, chronic, gastro-intestinal cases to later stages and the autopsy table. It is a clinical picture arising early or late in a variety of wasting diseases, particularly in those actively attacking the gastro-intestinal tract. However, this condition only interests us in this paper in its connection with amœbic disease, which, however, includes the majority of cases encountered in the Philippine Islands. It may appear somewhat early, but more usually late in the amœbiasis and often long after all evidences of the amœbic infection have disappeared. It is particularly liable to develop in those cases of amœbiasis complicated by disturbances of the stomach and small bowel, which have already been discussed. The symptomatology is so simple and has been so frequently described that it need not be noticed here. The salient points in the pathology were given by Woolley and Musgrave. A more complete study of both symptomatology and pathology would lead to a consideration of the diseases concerned in its multiple etiology; such a consideration has always been avoided by those classing it as a distinct disease. It is one of the most intractible conditions to treat which is found in the Tropics. This might be expected when we remember the principal pathologic changes found at autopsy, particularly the enlarged, thin-walled intestine, with atrophied cystic and often papiloid condition of the mucosa of the whole gastro-intestinal tube and the relaxation and partial destruction of the muscular bands of the bowel, which leave it elongated (often increased in length to 2–4 meters), enlarged in diameter, and without its natural folds and rugæ. Change of climate is necessary in most well-established cases in order to secure satisfactory results in treatment. Chronic gastro-enteritis does not of course always give rise to symptoms of sprue. This depends somewhat upon the nature of the etiologic factor and more upon the character of the fermenting bacteria, yeasts, and other substances multiplying in the bowel.

Abdominal pain and soreness persisting for years after amœbiasis, is quite a common sequel, and this condition is particularly frequent in patients who have had severe and prolonged attacks. It is undoubtedly due to areas of chronic adhesive peritonitis formed during the active stages of the disease. The symptomatology varies with the character and location of the adhesions. The clinical features may resemble a chronic appendicitis, when at autopsy none is found. Pains in the region of the liver, spleen, stomach, ovaries, and many other locations are met with. By far the most common character of the pain is one of general abdominal soreness, which is increased when the patient is in the erect posture and is relieved by his lying down. Just the reverse of this is also seen, in

which patients are never comfortable in the recumbent position. These pains may last for years after the disappearance of the disease or they may recur, particularly after exposure to cold or after violent exercise. The writer was, for more than a year after recovery from amœbic infection, troubled with these pains, and even now, more than five years since the original disease, a chilling of the abdomen, a slight diarrhœa, or an active cathartic will cause a recurrence of some pain. Treatment of the condition is not, as a rule, satisfactory. Carefully regulated exercise and massage may hasten the adjustment to new conditions and, sometimes with splanchnoptosis, proper bandages and corsets might advance a favorable result.

A considerable number of diseases and conditions already discussed under complications, particularly those appearing late in the disease, show their most decided results as after effects of amœbiasis. Among these are different types of gastro-intestinal disturbances in addition to sprue, chronic rheumatism, various disturbances of the nervous system, genito-urinary system, skin, etc. Therefore, the after picture is a very varied one; complete restoration to health is the most frequent outcome, but many of these cases go through life crippled by every complication which may be seen in other chronic, wasting diseases. The patients for the greater part disappear from the Tropics, but an extensive visit throughout the United States and careful scrutiny of our increasing pension roll will show us some of the awful ravages which this worst of all parasitic diseases is making on the American colonizers of the Tropics.[10]

[10] The inadvertent omission of the discussion of amœbic infection of the urinary bladder from this article has only been noticed in reading the proof. This subject was discussed by McDill and Musgrave in *Medical News*, December 16, 1905, page 1163. It will shortly again be taken up with the report of six more cases.

REVIEWS.

A Vocabulary of Malay Medical Terms. By P. N. Gerrard, B. A., BCH., B. A. O., M. D., Dub. Univ., D. T. M. H., Univ. Cantab. Pp. 107, Singapore: Kelly & Walsh, Limited. 1905.

This work is a well-written vocabulary of Malay medical phrases and terms. European and American physicians in the East have to depend almost entirely upon bedside diagnosis. The author has here presented definitions and interpretations in a concise form. The subjects of his conversations include some of the important diseases of the country, thus affording to physicians an easy method of procuring a clinical history, frequently a valuable asset in diagnosis.

M. T. C.